

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
8 July 2004 (08.07.2004)

PCT

(10) International Publication Number
WO 2004/056825 A1

(51) International Patent Classification⁷: C07D 471/04,
A01N 43/90

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(21) International Application Number:
PCT/GB2003/005250

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(22) International Filing Date: 3 December 2003 (03.12.2003)

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(26) Publication Language: English

Published:

- with international search report
- with amended claims

(30) Priority Data:
0230020.0 23 December 2002 (23.12.2002) GB

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

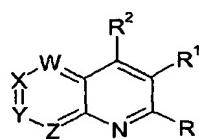
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WO 2004/056825 A1

(54) Title: PYRIDODIAZINES AS PLANT FUNGICIDES



(1)

(57) Abstract: Fungicidal compounds of general formula (1) wherein R, R¹, R², W, X, Y and Z are as defined in the specification.

PYRIDODIAZINES AS PLANT FUNGICIDES

This invention relates to novel derivatives of pyridopyrazines and pyridopyridazines, to processes for preparing them, to certain intermediate chemicals used in their manufacture, to compositions containing them and to methods of using them to combat fungi, especially 5 fungal infections of plants.

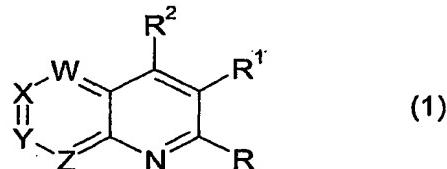
Derivatives of the nitrogen-containing 5,6 ring system *s*-1,2,4-triazolo[1,5-a]pyrimidine are known from the patent literature as being useful for controlling phytopathogenic fungi. Examples of recent patent publications include EP-A-1249452, WO 02/051845, WO 02/083676, WO 02/083677, WO 02/088125, WO 02/088126, WO 02/088127.

10 Derivatives of pyridopyrazines are known in the chemical literature, for example from *J. Med. Chem.* (1968), 11(6), 1216-18, *J. Med. Chem.* (1970), 13(5), 853-7 and US 3984412, but not for agrochemical purposes.

The present invention is concerned with the provision of novel pyridopyrazines and pyridopyridazines for combating phytopathogenic diseases on plants and harvested food

15 crops.

Thus, according to the present invention, there is provided a compound of the general formula (1):



20 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;

R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;

R and R² are independently H, halo, C₁₋₈ alkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio, C₂₋₈ alkenyl, C₂₋₈ alkynyl, cyano or NR³R⁴, provided that at least one of R and R² is NR³R⁴;

25 R¹ is halo, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C₁₋₄)alkyl, aryl(C₁₋₄)alkoxy, heteroaryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkoxy, aryl(C₁₋₄)-alkylthio, heteroaryl(C₁₋₄)alkylthio, morpholino, piperidino or pyrrolidino;

R³ and R⁴ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl,

30 C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₈)alkyl, NR⁵R⁶, provided

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that not both R³ and R⁴ are H or NR⁵R⁶, or

R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with one or more C₁₋₄ alkyl or C₁₋₄ alkoxy groups, or,

together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine,

5 thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring; and

R⁵ and R⁶ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₈)alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for

10 R⁸) being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆ alkoxy carbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or C₁₋₆ dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and

15 any of the foregoing aryl or heteroaryl groups or moieties being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyoxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, iso-
20 thiocyanato, nitro, -NR^{"R"}, -NHCOR^{"R"}, -NHCONR^{"R"}, -CONR^{"R"}, -SO₂R^{"R"}, -OSO₂R^{"R"}, -COR^{"R"}, -CR^{"R"}=NR^{"R"} or -N=CR^{"R"}, in which R^{"R"} and R^{"R"} are independently hydrogen, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.

25 The invention includes a compound of the general formula (1) as defined immediately above except that: C₁₋₈ alkoxy and C₁₋₈ alkylthio are excluded as values of R and R²; C₇ alkylene and C₃₋₇ alkenylene are excluded as chains formed by R³ and R⁴; the C₃₋₆ chain that R³ and R⁴ may form may only be optionally substituted with one or more methyl groups; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R³ and R⁴ may form; tri(C₁₋₄)alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

The compounds of the invention may contain one or more asymmetric carbon atoms and may exist as enantiomers (or as pairs of diastereoisomers) or as mixtures of such. They may also exist as diastereoisomers by virtue of restricted rotation about a bond. However, mixtures of enantiomers or diastereoisomers may be separated into individual isomers or 5 isomer pairs, and this invention embraces such isomers and mixtures thereof in all proportions. It is to be expected that for any given compound, one isomer may be more fungicidally active than another.

Except where otherwise stated, alkyl groups and alkyl moieties of alkoxy, alkylthio, etc., contain from 1 to 8, suitably from 1 to 6 and typically from 1 to 4, carbon atoms in the 10 form of straight or branched chains. Examples are methyl, ethyl, *n*- and *iso*-propyl, *n*-, *sec*-, *iso*- and *tert*-butyl, *n*-pentyl and *n*-hexyl. Cycloalkyl groups contain from 3 to 8, typically from 3 to 6, carbon atoms and include bicycloalkyl groups such as the bicyclo[2.2.1]heptyl group. Haloalkyl groups or moieties are typically trichloromethyl or trifluoromethyl or contain a trichloromethyl or trifluoromethyl terminal group.

15 Except where otherwise stated, alkenyl and alkynyl moieties also contain from 2 to 8, suitably from 2 to 6 and typically from 2 to 4, carbon atoms in the form of straight or branched chains. Examples are allyl, 2-methylallyl and propargyl. Optional substituents include halo, typically fluoro. An example of halo-substituted alkenyl is 3,4,4-trifluoro-*n*-butenyl.

20 Halo includes fluoro, chloro, bromo and iodo. Most commonly it is fluoro, chloro or bromo and usually fluoro or chloro.

Aryl is usually phenyl but also includes naphthyl, anthryl and phenanthryl.

Heteroaryl is typically a 5- or 6-membered aromatic ring containing one or more O, N or S heteroatoms, which may be fused to one or more other aromatic or heteroaromatic 25 rings, such as a benzene ring. Examples are thienyl, furyl, pyrrolyl, isoxazolyl, oxazolyl, oxadiazolyl, pyrazolyl, imidazolyl, triazolyl, isothiazolyl, tetrazolyl, thiadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, benzofuryl, benzothienyl, dibenzofuryl, benzothiazolyl, benzoxazolyl, benzimidazolyl, indolyl, quinolinyl and quinoxalinyl groups and, where appropriate, N-oxides thereof.

30 The 6,6-ring systems embraced by the general formula (1) are pyrido[2,3-*c*]pyridazines (where W and X are both CR⁸ and Y and Z are both N), pyrido[2,3-*d*]pyridazines (where W and Z are both CR⁸ and X and Y are both N), pyrido[3,2-*c*]pyridazines (where Y

and Z are both CR⁸ and W and X are both N) and pyrido[2,3-b]pyrazine (where X and Y are both CR⁸ and W and Z are both N). Of particular interest are pyrido[2,3-b]pyrazines.

R⁸, which may be the same or different for the two CR⁸ values of W, X, Y and Z, is H, halo (for example bromo), C₁₋₄ alkyl (for example methyl), C₁₋₄ alkoxy (for example methoxy) or halo(C₁₋₄)alkyl (for example trifluoromethyl). Usually R⁸ will be H.

One of R and R², preferably R², is NR³R⁴. The other is typically halo, especially chloro or fluoro. In the case of pyrido[2,3-b]pyrazine ring systems, the more active compounds are those where R² is NR³R⁴. R³ is typically C₁₋₈ alkyl (for example ethyl, n-propyl, n-butyl, sec-butyl (the S- or R-isomer or the racemate) and *tert*-butyl), halo(C₁₋₈)-alkyl (for example 2,2,2-trifluoroethyl, 2,2,2-trifluoro-1-methylethyl (the S- or R-isomer or the racemate), 3,3,3-trifluoropropyl and 4,4,4-trifluorobutyl), hydroxy(C₁₋₈)alkyl (for example hydroxyethyl), C₁₋₄ alkoxy(C₁₋₈)alkyl (for example methoxymethyl and methoxy-*iso*-butyl), C₁₋₄ alkoxyhalo(C₁₋₈)alkyl (for example 2-methoxy-2-trifluromethylethyl), tri-(C₁₋₄)alkylsilyl(C₁₋₆)alkyl (for example trimethylsilylmethyl), C₁₋₄ alkylcarbonyl(C₁₋₈)alkyl (for example 1-acetylethyl and 1-*tert*-butylcarbonylethyl), C₁₋₄ alkylcarbonylhalo(C₁₋₈)alkyl (for example 1-acetyl-2,2,2-trifluoroethyl), phenyl(C₁₋₄)alkyl (for example benzyl), C₂₋₈ alkenyl (for example allyl and methylallyl), halo(C₂₋₈)alkenyl (for example 3-methyl-4,4-difluorobut-3-enyl), C₂₋₈ alkynyl (for example propargyl), C₃₋₈ cycloalkyl (for example cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl) optionally substituted with chloro, fluoro or methyl, C₃₋₈ cycloalkyl(C₁₋₄)alkyl (for example cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl and cyclohexylmethyl), phenylamino, piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo (typically fluoro, chloro or bromo), C₁₋₄ alkyl (typically methyl), halo(C₁₋₄)alkyl (typically trifluoromethyl), C₁₋₄ alkoxy (typically methoxy) and halo(C₁₋₄)alkoxy (typically trifluoromethoxy). R⁴ is typically H, C₁₋₄ alkyl (for example ethyl and n-propyl), halo(C₁₋₄)alkyl (for example 2,2,2-trifluoroethyl) or amino. Alternatively R³ and R⁴ together form a C₄₋₆ alkylene chain optionally substituted with methyl, for example 3-methylpentylene, or, together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl.

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Typically R¹ is phenyl optionally substituted with from one to five halogen atoms, particularly fluorine and chlorine atoms and especially fluorine atoms or with from one to three substituents selected from halo (for example fluoro and chloro), C₁₋₄ alkyl (for example methyl), halo(C₁₋₄)alkyl (for example trifluoromethyl), C₁₋₄ alkoxy (for example methoxy) or halo(C₁₋₄)alkoxy (for example trifluoromethoxy). Examples are 2,6-difluorophenyl, 2-fluoro-6-chlorophenyl, 2,5,6-trifluorophenyl, 2,4,6-trifluorophenyl, 2,6-difluoro-4-methoxyphenyl, pentafluorophenyl, 2-fluorophenyl, 2,3,5,6-tetrafluorophenyl, 2-chloro-4,6-difluorophenyl, 2-chlorophenyl, 2,6-dichlorophenyl, 2,4-dichlorophenyl, 2,4,6-trichlorophenyl, 2,3,6-trichlorophenyl, pentachlorophenyl, 2-fluoro-4,6-dichlorophenyl, 4-fluoro-2,6-dichlorophenyl, 2-bromophenyl, 2-fluoro-6-bromophenyl, 2-bromo-4,6-difluorophenyl, 2-fluoro-6-methylphenyl, 2-chloro-6-methylphenyl, 2-methoxyphenyl, 2,6-dimethoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-trifluoromethylphenyl, 2-fluoro-6-trifluoromethylphenyl, 2,6-di-(trifluoromethyl)phenyl, 2-chloro-6-trifluoromethylphenyl, 2,4-difluoro-6-trifluoromethylphenyl, 2,4-difluoro-6-methoxyphenyl and 2,4-difluoro-6-methylphenyl.

Also of particular interest are compounds where R¹ is pyridyl optionally substituted with from one to four halogen atoms or with from one to three substituents selected from halo (for example fluoro and chloro), C₁₋₄ alkyl (for example methyl), halo(C₁₋₄)alkyl (for example trifluoromethyl), C₁₋₄ alkoxy (for example methoxy) or halo(C₁₋₄)alkoxy (for example trifluoromethoxy). Examples are 2,4-difluoropyrid-3-yl, 3,5-difluoropyrid-4-yl, tetrafluoropyrid-4-yl, 3-fluoropyrid-2-yl, 4-fluoropyrid-3-yl, 3-fluoropyrid-4-yl, 2-fluoropyrid-3-yl, 2,4,6-trifluoropyrid-3-yl, 3,5-difluoropyrid-2-yl, 2,6-difluoropyrid-3-yl, 2,4-difluoro-6-methoxypyrid-3-yl, 2-fluoro-4-chloropyrid-3-yl, 3-fluoro-5-chloropyrid-4-yl, 2-chloro-4-fluoropyrid-3-yl, 2,4-dichloropyrid-3-yl, 3-chloropyrid-2-yl I, 4-chloropyrid-3-yl, 3-chloropyrid-4-yl, 2-chloropyrid-3-yl, 3-trifluoromethylpyrid-2-yl, 4-trifluoromethylpyrid-3-yl, 3,5-dichloropyrid-2-yl, 4,6-dichloropyrid-3-yl, 3-trifluoromethylpyrid-4-yl, 2-trifluoromethylpyrid-3-yl, 2-fluoro-4-trifluoromethylpyrid-3-yl, 3-fluoro-5-trifluoromethylpyrid-4-yl, 4-fluoro-2-trifluoromethylpyrid-3-yl, 2,6-dichloropyrid-3-yl, 3,5-dichloropyrid-4-yl, 3-chloro-6-trifluoromethylpyrid-2-yl, 3-fluoro-6-trifluoromethylpyrid-2-yl, pyrid-2-yl, pyrid-3-yl and pyrid-4-yl.

Also of particular interest are compounds where R¹ is 2- or 3-thienyl optionally substituted with from one to three halogen atoms or with from one to three substituents selected from halo (for example fluoro and chloro), C₁₋₄ alkyl (for example methyl), halo(C₁₋₄)alkyl (for example trifluoromethyl), C₁₋₄ alkoxy (for example methoxy) or halo(C₁₋₄)-

alkoxy (for example trifluoromethoxy). Examples are 3-fluorothien-2-yl, 3-chlorothien-2-yl, 2,4-difluorothien-3-yl, 2,4-dichlorothien-3-yl and 2,4,5-trichlorothien-3-yl.

Examples of other values of R¹ of especial interest are unsubstituted piperidino and morpholino, 2-methylpiperidino, 2,6-dimethylpiperidino and 2,6-dimethylmorpholino.

- 5 In one aspect the invention provides a compound of the general formula (1) wherein W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;
- R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;
- one of R and R² (preferably R²) is NR³R⁴ and the other is halo;
- R¹ is halo, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl,
- 10 C₁₋₈ alkoxy, C₁₋₈ alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C₁₋₄)alkyl, aryl(C₁₋₄)alkoxy, heteroaryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkoxy, aryl(C₁₋₄)-alkylthio, heteroaryl(C₁₋₄)alkylthio, morpholino, piperidino or pyrrolidino;
- R³ and R⁴ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₈)alkyl, NR⁵R⁶, provided
- 15 that not both R³ and R⁴ are H or NR⁵R⁶, or
- R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with one or more C₁₋₄ alkyl or C₁₋₄ alkoxy groups, or,
- together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or
- 20 piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring; and
- R⁵ and R⁶ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₈)alkyl;
- any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R⁸) being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆ alkoxy carbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or C₁₋₆ dialkylamino,
- 25 any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and
- any of the foregoing aryl, heteroaryl, aryloxy or heteroaryl groups being optionally
- 30 substituted with one or more substituents selected from halo, hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano,

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isocyano, thiocyanato, isothiocyanato, nitro, -NR¹"R²", -NHCOR¹", -NHCONR¹"R²", -CONR¹"R²", -SO₂R¹", -OSO₂R¹", -COR¹", -CR¹=NR²" or -N=CR¹"R²", in which R¹" and R²" are independently hydrogen, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.

5 Of particular interest are compounds where W and Z are both N and X and Y are both CH.

The invention includes a compound of the general formula (1) as defined immediately above except that: C₇ alkylene and C₃₋₇ alkenylene are excluded as chains formed by R³ and R⁴; the C₃₋₆ chain that R³ and R⁴ may form may only be optionally 10 substituted with one or more methyl groups; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R³ and R⁴ may form; tri(C₁₋₄)alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

In another aspect the invention provides a compound of the general formula (1)
15 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;
R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;
one of R and R² (preferably R²) is NR³R⁴ and the other is halo;
R¹ is halo, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl,
20 C₁₋₈ alkoxy, C₁₋₈ alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio,
aryl(C₁₋₄)alkyl, aryl(C₁₋₄)alkoxy, heteroaryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkoxy, aryl(C₁₋₄)-
alkylthio, heteroaryl(C₁₋₄)alkylthio, morpholino, piperidino or pyrrolidino;
R³ is C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₂₋₄ alkenyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl or
phenylamino in which the phenyl ring is optionally substituted with one, two or three sub-
25 tituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy and halo(C₁₋₄)alkoxy; and
R⁴ is H, C₁₋₄ alkyl or amino, or
R³ and R⁴ together form a C₄₋₆ alkylene chain optionally substituted with C₁₋₄ alkyl or C₁₋₄
alkoxy, or,
together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine,
30 thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or
piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring;
any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for
R⁸) being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆

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alkoxycarbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or C₁₋₆ dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and

- 5 any of the foregoing aryl or heteroaryl groups or moieties being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, iso-
- 10 thiocyanato, nitro, -NR^{"R"}, -NHCOR^{"R"}, -NHCONR^{"R"}, -CONR^{"R"}, -SO₂R["], -OSO₂R["], -COR["], -CR["]=NR["] or -N=CR^{"R"}, in which R["] and R^{"'} are independently hydrogen, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.

- 15 Of particular interest are compounds where W and Z are both N and X and Y are both CH.

The invention includes a compound of the general formula (1) as defined immediately above except that: the C₄₋₆ chain that R³ and R⁴ may form may only be optionally substituted with methyl; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R³ and R⁴ may form; tri(C₁₋₄)alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

In yet another aspect the invention provides a compound of the general formula (1) wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;

- 25 R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;

R and R² are independently H, halo, C₁₋₈ alkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio, C₂₋₈ alkenyl, C₂₋₈ alkynyl, cyano or NR³R⁴, provided that at least one of R and R² (preferably R²) is NR³R⁴;

R¹ is optionally substituted phenyl;

R³ and R⁴ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl,

- 30 C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₈)alkyl, NR⁵R⁶, provided that not both R³ and R⁴ are H or NR⁵R⁶, or

R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with one or more C₁₋₄ alkyl or C₁₋₄ alkoxy groups, or,

- together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring; and
- R⁵ and R⁶ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, 5 C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₈)alkyl; any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R⁸) being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆ alkoxy carbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or C₁₋₆ dialkylamino,
- 10 any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and any of the foregoing aryl or heteroaryl groups or moieties, including the phenyl group of R¹, being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyoxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy-(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR^{"R"}, -NHCOR^{"R"}, -NHCONR^{"R"}, -CONR^{"R"}, -SO₂R["], -OSO₂R["], -COR["], -CR["]=NR["] or -N=CR^{"R"}, in which R["] and R^{"'} are independently hydrogen, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, 15 C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy. Of particular interest are compounds where W and Z are both N and X and Y are both CH.
- 20

The invention includes a compound of the general formula (1) as defined immediately above except that: C₁₋₈ alkoxy and C₁₋₈ alkylthio are excluded as values of R and R²; C₇ alkylene and C₃₋₇ alkenylene are excluded as chains formed by R³ and R⁴; the C₃₋₆ chain that R³ and R⁴ may form may only be optionally substituted with one or more methyl groups; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R³ and R⁴ may form; tri(C₁₋₄)alkylsilyl is excluded as a substituent 25 of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and the morpholine ring that R³ and R⁴ may form is unsubstituted.

In still yet another aspect the invention provides a compound of the general formula (1) wherein

- 10 -

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;

R⁸ is H, halo(e.g. fluoro, chloro or bromo), C₁₋₄ alkyl (e.g. methyl), C₁₋₄ alkoxy (e.g. methoxy) or halo(C₁₋₄)alkyl (e.g. trifluoromethyl);

R is H, halo (e.g. fluoro, chloro or bromo), C₁₋₄ alkyl (e.g. methyl), C₁₋₄ alkoxy (e.g. methoxy) or cyano;

5 R¹ is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)-alkoxy, pyridyl optionally substituted with from one to four halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)-alkoxy, 2- or 3-thienyl optionally substituted with from one to three halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkoxy, or piperidino or morpholino both optionally substituted with one or two methyl groups;

R² is NR³R⁴;

10 15 R³ is C₁₋₈ alkyl, halo(C₁₋₈)alkyl, hydroxy(C₁₋₈)alkyl, C₁₋₄ alkoxy(C₁₋₈)alkyl, C₁₋₄ alkoxyhalo-(C₁₋₈)alkyl, tri(C₁₋₄)alkylsilyl(C₁₋₆)alkyl, C₁₋₄ alkylcarbonyl(C₁₋₈)alkyl, C₁₋₄ alkylcarbonyl-halo(C₁₋₈)alkyl, phenyl(C₁₋₄)alkyl, C₂₋₈ alkenyl, halo(C₂₋₈)alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl optionally substituted with chloro, fluoro or methyl, C₃₋₈ cycloalkyl(C₁₋₄)alkyl, phenylamino, piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl,

20 C₁₋₄ alkoxy and halo(C₁₋₄)alkoxy; and

R⁴ is H, C₁₋₄ alkyl, halo(C₁₋₄)alkyl or amino, or

25 R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with methyl, or,

together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl.

Of particular interest are compounds where W and Z are both N and X and Y are both CH.

30 In still yet another aspect the invention provides a compound of the general formula (1) wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;

R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;

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R is halo;

R¹ is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)-alkoxy;

5 R² is NR³R⁴;

R³ is C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₂₋₄ alkenyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl or phenylamino in which the phenyl ring is optionally substituted with one, two or three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy and halo(C₁₋₄)alkoxy; and

10 R⁴ is H, C₁₋₄ alkyl or amino, or R³ and R⁴ together form a C₄₋₆ alkylene chain optionally substituted with methyl, or, together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine ring.

Of particular interest are compounds where W and Z are both N and X and Y are both CH.

Compounds that form part of the invention are illustrated in Tables 1 to 127 below.

15 Characterising data are given later in the Examples and in Table 133.

In Table 1 the compounds have the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2,4,6-trifluorophenyl and R³ and R⁴ are as shown in the table.

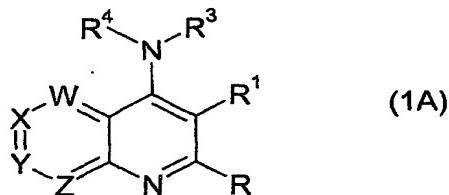


Table 1

Cmpd No	R ³	R ⁴
1	C ₂ H ₅	H
2	n-C ₃ H ₇	H
3	i-C ₃ H ₇	H
4	n-C ₄ H ₉	H
5	t-C ₄ H ₉	H
6	CH ₂ =CHCH ₂	H
7	CH ₂ =C(CH ₃)CH ₂	H
8	CF ₃ CH ₂	H
9	CF ₃ CH ₂ CH ₂	H
10	CF ₃ CH ₂ CH ₂ CH ₂	H

Cmpd No	R ³	R ⁴
11	CF ₃ (CH ₃)CH	H
12	(S)-CF ₃ (CH ₃)CH	H
13	(R)-CF ₃ (CH ₃)CH	H
14	cyclo-C ₃ H ₅	H
15	cyclo-C ₄ H ₇	H
16	cyclo-C ₅ H ₉	H
17	cyclo-C ₆ H ₁₁	H
18	cyclo-C ₃ H ₅ CH ₂	H
19	cyclo-C ₄ H ₇ CH ₂	H
20	-(CH ₂) ₂ O(CH ₂) ₂ -	

Cmpd No	R ³	R ⁴
21	cyclo-C ₆ H ₁₁ CH ₂	H
22	-(CH ₂) ₂ CH(CH ₃)(CH ₂) ₂ -	
23	CH ₃ CH ₂ (CH ₃)CH	H
24	(S)-CH ₃ CH ₂ (CH ₃)CH	H
25	(R)-CH ₃ CH ₂ (CH ₃)CH	H
26	C ₂ H ₅	C ₂ H ₅
27	n-C ₃ H ₇	n-C ₃ H ₇
28	CH ₂ =C(CH ₃)CH ₂	C ₂ H ₅
29	CF ₃ CH ₂	C ₂ H ₅
30	C ₂ H ₅	NH ₂
31	n-C ₃ H ₇	NH ₂
32	i-C ₃ H ₇	NH ₂
33	n-C ₄ H ₉	NH ₂
34	CH ₂ =CHCH ₂	NH ₂
35	CH ₂ =C(CH ₃)CH ₂	NH ₂
36	CF ₂ =CFCH ₂ CH ₂	NH ₂
37	CF ₃ CH ₂	NH ₂
38	CF ₃ CH ₂ CH ₂	NH ₂
39	CF ₃ CH ₂ CH ₂ CH ₂	NH ₂
40	4-t-C ₄ H ₉ -C ₆ H ₄ NH	H
41	4-F-C ₆ H ₄ NH	H
42	C ₆ H ₅ NH	H
43	4-CH ₃ -C ₆ H ₄ NH	H
44	4-Br-C ₆ H ₄ NH	H
45	2-F-C ₆ H ₄ NH	H
46	3,4-Cl ₂ -C ₆ H ₃ NH	H
47	3-CF ₃ -C ₆ H ₄ NH	H
48	3,5-Cl ₂ -C ₆ H ₃ NH	H
49	4-CF ₃ O-C ₆ H ₅ NH	H
50	2-CF ₃ -C ₆ H ₄ NH	H
51	4-CF ₃ -C ₆ H ₄ NH	H
52	2-Br-C ₆ H ₄ NH	H
53	2-Cl-C ₆ H ₄ NH	H
54	2-CH ₃ -4-Cl-C ₆ H ₃ NH	H
55	2-CH ₃ -5-F-C ₆ H ₃ NH	H
56	3-Cl-C ₆ H ₄ NH	H
57	CH ₃	H

Cmpd No	R ³	R ⁴
58	(CH ₃) ₂ CHCH ₂	H
59	(CH ₃) ₃ CCH ₂	H
60	(CH ₃) ₃ C(CH ₃)CH	H
61	CH ₃ CH ₂ (CH ₃) ₂ C	H
62	CH ₃ CH ₂ (CF ₃)CH	H
63	(S)-CH ₃ CH ₂ (CF ₃)CH	H
64	(R)-CH ₃ CH ₂ (CF ₃)CH	H
65	CH ₃ CH ₂ (CH ₃ CH ₂)CH	H
66	(CH ₃) ₂ CH(CH ₃ CH ₂)CH	H
67	(CH ₃) ₂ CH(CH ₃)CH	H
68	(CH ₃) ₂ CH(CF ₃)CH	H
69	(S)-(CH ₃) ₂ CH(CF ₃)CH	H
70	(R)-(CH ₃) ₂ CH(CF ₃)CH	H
71	HC=C(CH ₃)CH ₂	H
72	CH ₂ =CH(CH ₃ CH ₂)CH	H
73	CH ₃ CH ₂ CH ₂ (CH ₃)CH	H
74	CH ₃ CH ₂ CH ₂ (CF ₃)CH	H
75	(S)-CH ₃ CH ₂ CH ₂ (CF ₃)CH	H
76	(R)-CH ₃ CH ₂ CH ₂ (CF ₃)CH	H
77	CH ₃ CH ₂ CH ₂ (CH ₃) ₂ C	H
78	CH ₃ CH ₂ (CH ₃)CHCH ₂	H
79	(CH ₃) ₂ CHCH ₂ CH ₂	H
80	(CH ₃) ₃ CCH ₂ CH ₂	H
81	CH ₃ CH ₂ (CH ₃)CH(CH ₃)-CH	H
82	CH ₃ CH ₂ (CH ₃)CH(CF ₃)-CH	H
83	(S)-CH ₃ CH ₂ (CH ₃)CH-(CF ₃)CH	H
84	(R)-CH ₃ CH ₂ (CH ₃)CH-(CF ₃)CH	H
85	CH ₃ (CH ₃)CHCH ₂ (CH ₃)-CH	H
86	CH ₃ (CH ₃)CHCH ₂ (CF ₃)-CH	H
87	(S)-CH ₃ (CH ₃)CHCH ₂ -(CF ₃)CH	H
88	(R)-CH ₃ (CH ₃)CHCH ₂ -(CF ₃)CH	H
89	(CH ₃) ₂ CH(CH ₃)CH-(CH ₃)CH ₂	H
90	(CH ₃) ₃ CCH ₂ (CH ₃)CH	H
91	E-CH ₃ CH=CH(CH ₃)CH	H

Cmpd No	R ³	R ⁴
92	E-CH ₃ CH=CH(CH ₃ CH ₂)-CH	H
93	CH ₃ CH ₂ CH ₂ (CH ₃ CH ₂)-CH	H
94	CH ₃ CH ₂ (CH ₃ CH ₂)-CHCH ₂	H
95	CF ₂ =CFCH ₂ CH ₂	H
96	CF ₃ CH ₂ (CH ₃)CHCH ₂	H
97	CF ₃ CF ₂ CH ₂ CH ₂	H
98	CF ₃ CF ₂ CF ₂ CH ₂	H
99	CF ₂ =C(CH ₃)CH ₂ CH ₂	H
100	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂	H
101	CH ₃ CH ₂ CH ₂ CH ₂ -(CH ₃)CH	H
102	CH ₃ CH ₂ CH ₂ (CH ₃)-CHCH ₂	H
103	CH ₃ CH ₂ (CH ₃)CHCH ₂ -CH ₂	H
104	CH ₃ CH ₂ CH ₂ (CH ₃)CH-(CH ₃)CH	H
105	CH ₃ CH ₂ (CH ₃)CHCH ₂ -(CH ₃)CH	H
106	HOCH ₂ CH ₂	H
107	CH ₃ OCH ₂ CH ₂	H
108	CH ₃ OCH ₂ (CH ₃)CH	H
109	CH ₃ OCH ₂ (CF ₃)CH	H
110	CH ₃ OCH ₂ (CH ₃) ₂ C	H
111	CH ₃ O(CH ₃)CHCH ₂	H
112	CH ₃ O(CH ₃)CH(CH ₃)CH	H
113	HC≡CCH ₂	H
114	CH ₃ C≡CCH ₂	H
115	HC≡CCH ₂ CH ₂	H
116	HOCH ₂ CH ₂ CH ₂	H
117	CH ₃ OCH ₂ CH ₂ CH ₂	H
118	(CH ₃) ₃ SiCH ₂	H
119	C ₆ H ₅ CH ₂	H
120	C ₆ H ₅ (CH ₃)CH	H
121	4-F-C ₆ H ₄ CH ₂	H
122	4-Cl-C ₆ H ₄ CH ₂	H
123	4-F-C ₆ H ₅ (CH ₃)CH	H
124	4-Cl-C ₆ H ₅ (CH ₃)CH	H
125	C ₆ H ₅ CH ₂ CH ₂	H

Cmpd No	R ³	R ⁴
126	4-F-C ₆ H ₅ CH ₂ CH ₂	H
127	1-piperidino	H
128	1-pyrrolidino	H
129	cyclo-C ₅ H ₉ CH ₂	H
130	Bicyclo[2.2.1]hept-2-yl	H
131	1-CH ₃ -cyclopropyl	H
132	cis-2-CH ₃ -cyclopropyl	H
133	trans-2-CH ₃ -cyclopropyl	H
134	2,2-(CH ₃) ₂ -cyclopropyl	H
135	1-CH ₃ -cyclobutyl	H
136	cis-2-CH ₃ -cyclobutyl	H
137	trans-2-CH ₃ -cyclobutyl	H
138	cis-3-CH ₃ -cyclobutyl	H
139	trans-3-CH ₃ -cyclobutyl	H
140	2,2-(CH ₃) ₂ -cyclobutyl	H
141	3,3-(CH ₃) ₂ -cyclobutyl	H
142	1-CH ₃ -cyclopentyl	H
143	cis-2-CH ₃ -cyclopentyl	H
144	trans-2-CH ₃ -cyclopentyl	H
145	cis-3-CH ₃ -cyclopentyl	H
146	trans-3-CH ₃ -cyclopentyl	H
147	2,2-(CH ₃) ₂ -cyclopentyl	H
148	3,3-(CH ₃) ₂ -cyclopentyl	H
149	1-CH ₃ -cyclohexyl	H
150	cis-2-CH ₃ -cyclohexyl	H
151	trans-2-CH ₃ -cyclohexyl	H
152	cis-3-CH ₃ -cyclohexyl	H
153	trans-3-CH ₃ -cyclohexyl	H
154	2,2-(CH ₃) ₂ -cyclohexyl	H
155	3,3-(CH ₃) ₂ -cyclohexyl	H
156	cis-4-CH ₃ -cyclohexyl	H
157	trans-4-CH ₃ -cyclohexyl	H
158	4,4-(CH ₃) ₂ -cyclohexyl	H
159	4-(CH ₃) ₃ C-cyclohexyl	H
160	-(CH ₂) ₃ -	
161	-(CH ₂) ₄ -	
162	-(CH ₂) ₅ -	

Cmpd No	R ³	R ⁴
163	-(CH ₂) ₆ -	
164	-(CH ₂) ₂ (CH ₃) ₂ C(CH ₂) ₂ -	
165	-(CH ₃)CH(CH ₂) ₂ -	
166	-(CH ₃)CH(CH ₂) ₃ -	
167	-(CH ₃)CH(CH ₂) ₄ -	
168	-(CH ₃)CH(CH ₂) ₅ -	
169	-CH ₂ CH=CH(CH ₂) ₂ -	
170	-(CH ₂) ₂ NH(CH ₂) ₂ -	
171	-(CH ₂) ₂ NCH ₃ (CH ₂) ₂ -	
172	-(CH ₂) ₂ S(CH ₂) ₂ -	
173	-(CH ₂) ₂ SO(CH ₂) ₂ -	
174	-(CH ₂) ₂ SO ₂ (CH ₂) ₂ -	
175	-CH ₂ (CH ₃)CHO(CH ₃)CHCH ₂ -	
176	C ₂ H ₅	CH ₃
177	n-C ₃ H ₇	CH ₃
178	i-C ₃ H ₇	CH ₃
179	n-C ₄ H ₉	CH ₃
180	t-C ₄ H ₉	CH ₃
181	CH ₂ =CHCH ₂	CH ₃
182	CH ₂ =C(CH ₃)CH ₂	CH ₃
183	CF ₃ CH ₂	CH ₃
184	CF ₃ CH ₂ CH ₂	CH ₃
185	CF ₃ CH ₂ CH ₂ CH ₂	CH ₃
186	CF ₃ (CH ₃)CH	CH ₃
187	(S)-CF ₃ (CH ₃)CH	CH ₃
188	(R)-CF ₃ (CH ₃)CH	CH ₃
189	cyclo-C ₃ H ₅	CH ₃
190	cyclo-C ₄ H ₇	CH ₃
191	cyclo-C ₅ H ₉	CH ₃
192	cyclo-C ₆ H ₁₁	CH ₃
193	cyclo-C ₃ H ₅ CH ₂	CH ₃
194	cyclo-C ₄ H ₇ CH ₂	CH ₃
195	cyclo-C ₆ H ₁₁ CH ₂	CH ₃
196	CH ₃ CH ₂ (CH ₃)CH	CH ₃
197	(S)-CH ₃ CH ₂ (CH ₃)CH	CH ₃
198	(R)-CH ₃ CH ₂ (CH ₃)CH	CH ₃
199	cyclo-C ₇ H ₁₃	CH ₃

Cmpd No	R ³	R ⁴
200	CH ₂ =C(CH ₃)CH ₂	CH ₃
201	CF ₃ CH ₂	CH ₃
202	4-t-C ₄ H ₉ -C ₆ H ₄ NH	CH ₃
203	4-F-C ₆ H ₄ NH	CH ₃
204	C ₆ H ₅ NH	CH ₃
205	4-CH ₃ -C ₆ H ₄ NH	CH ₃
206	4-Br-C ₆ H ₄ NH	CH ₃
207	2-F-C ₆ H ₄ NH	CH ₃
208	3,4-Cl ₂ -C ₆ H ₃ NH	CH ₃
209	3-CF ₃ -C ₆ H ₄ NH	CH ₃
210	3,5-Cl ₂ -C ₆ H ₃ NH	CH ₃
211	4-CF ₃ O-C ₆ H ₅ NH	CH ₃
212	2-CF ₃ -C ₆ H ₄ NH	CH ₃
213	4-CF ₃ -C ₆ H ₄ NH	CH ₃
214	2-Br-C ₆ H ₄ NH	CH ₃
215	2-Cl-C ₆ H ₄ NH	CH ₃
216	2-CH ₃ -4-Cl-C ₆ H ₃ NH	CH ₃
217	2-CH ₃ -5-F-C ₆ H ₃ NH	CH ₃
218	3-Cl-C ₆ H ₄ NH	CH ₃
219	CH ₃	CH ₃
220	(CH ₃) ₂ CHCH ₂	CH ₃
221	(CH ₃) ₃ CCH ₂	CH ₃
222	(CH ₃) ₃ C(CH ₃)CH	CH ₃
223	CH ₃ CH ₂ (CH ₃) ₂ C	CH ₃
224	CH ₃ CH ₂ (CF ₃)CH	CH ₃
225	(S)-CH ₃ CH ₂ (CF ₃)CH	CH ₃
226	(R)-CH ₃ CH ₂ (CF ₃)CH	CH ₃
227	CH ₃ CH ₂ (CH ₃ CH ₂)CH	CH ₃
228	(CH ₃) ₂ CH(CH ₃ CH ₂)CH	CH ₃
229	(CH ₃) ₂ CH(CH ₃)CH	CH ₃
230	(CH ₃) ₂ CH(CF ₃)CH	CH ₃
231	(S)-(CH ₃) ₂ CH(CF ₃)CH	CH ₃
232	(R)-(CH ₃) ₂ CH(CF ₃)CH	CH ₃
233	HC=C(CH ₃)CH ₂	CH ₃
234	CH ₂ =CH(CH ₃ CH ₂)CH	CH ₃
235	CH ₃ CH ₂ CH ₂ (CH ₃)CH	CH ₃
236	CH ₃ CH ₂ CH ₂ (CF ₃)CH	CH ₃

Cmpd No	R ³	R ⁴
237	(S)-CH ₃ CH ₂ CH ₂ (CF ₃)CH	CH ₃
238	(R)-CH ₃ CH ₂ CH ₂ (CF ₃)CH	CH ₃
239	CH ₃ CH ₂ CH ₂ (CH ₃) ₂ C	CH ₃
240	CH ₃ CH ₂ (CH ₃)CHCH ₂	CH ₃
241	(CH ₃) ₂ CHCH ₂ CH ₂	CH ₃
242	(CH ₃) ₃ CCH ₂ CH ₂	CH ₃
243	CH ₃ CH ₂ (CH ₃)CH(CH ₃)-CH	CH ₃
244	CH ₃ CH ₂ (CH ₃)CH(CF ₃)-CH	CH ₃
245	(S)-CH ₃ CH ₂ (CH ₃)CH-(CF ₃)CH	CH ₃
246	(R)-CH ₃ CH ₂ (CH ₃)CH-(CF ₃)CH	CH ₃
247	CH ₃ (CH ₃)CHCH ₂ -(CH ₃)CH	CH ₃
248	CH ₃ (CH ₃)CHCH ₂ -(CF ₃)CH	CH ₃
249	(S)-CH ₃ (CH ₃)CHCH ₂ -(CF ₃)CH	CH ₃
250	(R)-CH ₃ (CH ₃)HCH ₂ -(CF ₃)CH	CH ₃
251	(CH ₃) ₂ CH(CH ₃)CH(CH ₃)-CH ₂	CH ₃
252	(CH ₃) ₃ CCH ₂ (CH ₃)CH	CH ₃
253	E-CH ₃ CH=CH(CH ₃)CH	CH ₃
254	E-CH ₃ CH=CH(CH ₃ CH ₂)-CH	CH ₃
255	CH ₃ CH ₂ CH ₂ (CH ₃ CH ₂)-CH	CH ₃
256	CH ₃ CH ₂ (CH ₃ CH ₂)-CHCH ₂	CH ₃
257	CF ₂ =CFCH ₂ CH ₂	CH ₃
258	CF ₃ CH ₂ (CH ₃)CHCH ₂	CH ₃
259	CF ₃ CF ₂ CH ₂ CH ₂	CH ₃
260	CF ₃ CF ₂ CF ₂ CH ₂	CH ₃
261	CF ₂ =C(CH ₃)CH ₂ CH ₂	CH ₃
262	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂	CH ₃
263	CH ₃ CH ₂ CH ₂ CH ₂ (CH ₃)-CH	CH ₃
264	CH ₃ CH ₂ CH ₂ (CH ₃)-CHCH ₂	CH ₃
265	CH ₃ CH ₂ (CH ₃)CHCH ₂ -CH ₂	CH ₃
266	CH ₃ CH ₂ CH ₂ (CH ₃)CH-(CH ₃)CH	CH ₃
267	CH ₃ CH ₂ (CH ₃)CHCH ₂ -(CH ₃)CH	CH ₃

Cmpd No	R ³	R ⁴
268	HOCH ₂ CH ₂	CH ₃
269	CH ₃ OCH ₂ CH ₂	CH ₃
270	CH ₃ OCH ₂ (CH ₃)CH	CH ₃
271	CH ₃ OCH ₂ (CF ₃)CH	CH ₃
272	CH ₃ OCH ₂ (CH ₃) ₂ C	CH ₃
273	CH ₃ O(CH ₃)CHCH ₂	CH ₃
274	CH ₃ O(CH ₃)CH(CH ₃)CH	CH ₃
275	HC≡CCH ₂	CH ₃
276	CH ₃ C≡CCH ₂	CH ₃
277	HC≡CCH ₂ CH ₂	CH ₃
278	HOCH ₂ CH ₂ CH ₂	CH ₃
279	CH ₃ OCH ₂ CH ₂ CH ₂	CH ₃
280	(CH ₃) ₃ SiCH ₂	CH ₃
281	C ₆ H ₅ CH ₂	CH ₃
282	C ₆ H ₅ (CH ₃)CH	CH ₃
283	4-F-C ₆ H ₄ CH ₂	H
284	4-Cl-C ₆ H ₄ CH ₂	CH ₃
285	4-F-C ₆ H ₅ (CH ₃)CH	CH ₃
286	4-Cl-C ₆ H ₅ (CH ₃)CH	CH ₃
287	C ₆ H ₅ CH ₂ CH ₂	CH ₃
288	4-F-C ₆ H ₅ CH ₂ CH ₂	CH ₃
289	1-piperidino	CH ₃
290	1-pyrrolidino	CH ₃
291	cyclo-C ₅ H ₉ CH ₂	CH ₃
292	bicyclo[2.2.1]hept-2-yl	CH ₃
293	1-CH ₃ -cyclopropyl	CH ₃
294	cis-2-CH ₃ -cyclopropyl	CH ₃
295	trans-2-CH ₃ -cyclopropyl	CH ₃
296	2,2-(CH ₃) ₂ -cyclopropyl	CH ₃
297	1-CH ₃ -cyclobutyl	CH ₃
298	cis-2-CH ₃ -cyclobutyl	CH ₃
299	trans-2-CH ₃ -cyclobutyl	CH ₃
300	cis-3-CH ₃ -cyclobutyl	CH ₃
301	trans-3-CH ₃ -cyclobutyl	CH ₃
302	2,2-(CH ₃) ₂ -cyclobutyl	CH ₃
303	3,3-(CH ₃) ₂ -cyclobutyl	CH ₃
304	1-CH ₃ -cyclopentyl	CH ₃

Cmpd No	R ³	R ⁴
305	<i>cis</i> -2-CH ₃ -cyclopentyl	CH ₃
306	<i>trans</i> -2-CH ₃ -cyclopentyl	CH ₃
307	<i>cis</i> -3-CH ₃ -cyclopentyl	CH ₃
308	<i>trans</i> -3-CH ₃ -cyclopentyl	CH ₃
309	2,2-(CH ₃) ₂ -cyclopentyl	CH ₃
310	3,3-(CH ₃) ₂ -cyclopentyl	CH ₃
311	1-CH ₃ -cyclohexyl	CH ₃
312	<i>cis</i> -2-CH ₃ -cyclohexyl	CH ₃
313	<i>trans</i> -2-CH ₃ -cyclohexyl	CH ₃
314	<i>cis</i> -3-CH ₃ -cyclohexyl	CH ₃
315	<i>trans</i> -3-CH ₃ -cyclohexyl	CH ₃
316	2,2-(CH ₃) ₂ -cyclohexyl	CH ₃
317	3,3-(CH ₃) ₂ -cyclohexyl	CH ₃
318	<i>cis</i> -4-CH ₃ -cyclohexyl	CH ₃
319	<i>trans</i> -4-CH ₃ -cyclohexyl	CH ₃
320	4,4-(CH ₃) ₂ -cyclohexyl	CH ₃
321	4-(CH ₃) ₃ C-cyclohexyl	CH ₃
322	<i>n</i> -C ₃ H ₇	C ₂ H ₅
323	<i>i</i> -C ₃ H ₇	C ₂ H ₅
324	<i>n</i> -C ₄ H ₉	C ₂ H ₅
325	<i>t</i> -C ₄ H ₉	C ₂ H ₅
326	CH ₂ =CHCH ₂	C ₂ H ₅
327	CF ₃ CH ₂ CH ₂	C ₂ H ₅
328	CF ₃ CH ₂ CH ₂ CH ₂	C ₂ H ₅
329	CF ₃ (CH ₃)CH	C ₂ H ₅
330	(S)-CF ₃ (CH ₃)CH	C ₂ H ₅
331	(R)-CF ₃ (CH ₃)CH	C ₂ H ₅
332	cyclo-C ₃ H ₅	C ₂ H ₅
333	cyclo-C ₄ H ₇	C ₂ H ₅
334	cyclo-C ₅ H ₉	C ₂ H ₅
335	cyclo-C ₆ H ₁₁	C ₂ H ₅
336	cyclo-C ₃ H ₅ CH ₂	C ₂ H ₅
337	cyclo-C ₄ H ₇ CH ₂	C ₂ H ₅
338	cyclo-C ₆ H ₁₁ CH ₂	C ₂ H ₅
339	CH ₃ CH ₂ (CH ₃)CH	C ₂ H ₅
340	(S)-CH ₃ CH ₂ (CH ₃)CH	C ₂ H ₅
341	(R)-CH ₃ CH ₂ (CH ₃)CH	C ₂ H ₅

Cmpd No	R ³	R ⁴
342	cyclo-C ₇ H ₁₃	C ₂ H ₅
343	4- <i>t</i> -C ₄ H ₉ -C ₆ H ₄ NH	C ₂ H ₅
344	4-F-C ₆ H ₄ NH	C ₂ H ₅
345	C ₆ H ₅ NH	C ₂ H ₅
346	4-CH ₃ -C ₆ H ₄ NH	C ₂ H ₅
347	4-Br-C ₆ H ₄ NH	C ₂ H ₅
348	2-F-C ₆ H ₄ NH	C ₂ H ₅
349	3,4-Cl ₂ -C ₆ H ₃ NH	C ₂ H ₅
350	3-CF ₃ -C ₆ H ₄ NH	C ₂ H ₅
351	3,5-Cl ₂ -C ₆ H ₃ NH	C ₂ H ₅
352	4-CF ₃ O-C ₆ H ₅ NH	C ₂ H ₅
353	2-CF ₃ -C ₆ H ₄ NH	C ₂ H ₅
354	4-CF ₃ -C ₆ H ₄ NH	C ₂ H ₅
355	2-Br-C ₆ H ₄ NH	C ₂ H ₅
356	2-Cl-C ₆ H ₄ NH	C ₂ H ₅
357	2-CH ₃ -4-Cl-C ₆ H ₃ NH	C ₂ H ₅
358	2-CH ₃ -5-F-C ₆ H ₃ NH	C ₂ H ₅
359	3-Cl-C ₆ H ₄ NH	C ₂ H ₅
360	(CH ₃) ₂ CHCH ₂	C ₂ H ₅
361	(CH ₃) ₃ CCH ₂	C ₂ H ₅
362	(CH ₃) ₃ C(CH ₃)CH	C ₂ H ₅
363	CH ₃ CH ₂ (CH ₃) ₂ C	C ₂ H ₅
364	CH ₃ CH ₂ (CF ₃)CH	C ₂ H ₅
365	(S)-CH ₃ CH ₂ (CF ₃)CH	C ₂ H ₅
366	(R)-CH ₃ CH ₂ (CF ₃)CH	C ₂ H ₅
367	CH ₃ CH ₂ (CH ₃ CH ₂)CH	C ₂ H ₅
368	(CH ₃) ₂ CH(CH ₃ CH ₂)CH	C ₂ H ₅
369	(CH ₃) ₂ CH(CH ₃)CH	C ₂ H ₅
370	(CH ₃) ₂ CH(CF ₃)CH	C ₂ H ₅
371	(S)-(CH ₃) ₂ CH(CF ₃)CH	C ₂ H ₅
372	(R)-(CH ₃) ₂ CH(CF ₃)CH	C ₂ H ₅
373	HC=C(CH ₃)CH ₂	C ₂ H ₅
374	CH ₂ =CH(CH ₃ CH ₂)CH	C ₂ H ₅
375	CH ₃ CH ₂ CH ₂ (CH ₃)CH	C ₂ H ₅
376	CH ₃ CH ₂ CH ₂ (CF ₃)CH	C ₂ H ₅
377	(S)-CH ₃ CH ₂ CH ₂ (CF ₃)CH	C ₂ H ₅
378	(R)-CH ₃ CH ₂ CH ₂ (CF ₃)CH	C ₂ H ₅

Cmpd No	R ³	R ⁴
379	CH ₃ CH ₂ CH ₂ (CH ₃) ₂ C	C ₂ H ₅
380	CH ₃ CH ₂ (CH ₃)CHCH ₂	C ₂ H ₅
381	(CH ₃) ₂ CHCH ₂ CH ₂	C ₂ H ₅
382	(CH ₃) ₂ CCH ₂ CH ₂	C ₂ H ₅
383	CH ₃ CH ₂ (CH ₃)CH(CH ₃)-CH	C ₂ H ₅
384	CH ₃ CH ₂ (CH ₃)CH(CF ₃)-CH	C ₂ H ₅
385	(S)-CH ₃ CH ₂ (CH ₃)CH-(CF ₃)-CH	C ₂ H ₅
386	(R)-CH ₃ CH ₂ (CH ₃)CH-(CF ₃)-CH	C ₂ H ₅
387	CH ₃ (CH ₃)CHCH ₂ (CH ₃)-CH	C ₂ H ₅
388	CH ₃ (CH ₃)CHCH ₂ (CF ₃)-CH	C ₂ H ₅
389	(S)-CH ₃ (CH ₃)CHCH ₂ -(CF ₃)-CH	C ₂ H ₅
390	(R)-CH ₃ (CH ₃)CHCH ₂ -(CF ₃)-CH	C ₂ H ₅
391	(CH ₃) ₂ CH(CH ₃)CH-(CH ₃)CH ₂	C ₂ H ₅
392	(CH ₃) ₃ CCH ₂ (CH ₃)CH	C ₂ H ₅
393	E-CH ₃ CH=CH(CH ₃)CH	C ₂ H ₅
394	E-C H ₃ CH=CH-(CH ₃ CH ₂)-CH	C ₂ H ₅
395	CH ₃ CH ₂ CH ₂ (CH ₃ CH ₂)-CH	C ₂ H ₅
396	CH ₃ CH ₂ (CH ₃ CH ₂)CH-CH ₂	C ₂ H ₅
397	CF ₂ =CFCH ₂ CH ₂	C ₂ H ₅
398	CF ₃ CH ₂ (CH ₃)CHCH ₂	C ₂ H ₅
399	CF ₃ CF ₂ CH ₂ CH ₂	C ₂ H ₅
400	CF ₃ CF ₂ CF ₂ CH ₂	C ₂ H ₅
401	CF ₂ =C(CH ₃)CH ₂ CH ₂	C ₂ H ₅
402	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂	C ₂ H ₅
403	CH ₃ CH ₂ CH ₂ CH ₂ (CH ₃)-CH	C ₂ H ₅
404	CH ₃ CH ₂ CH ₂ (CH ₃)CH-CH ₂	C ₂ H ₅
405	CH ₃ CH ₂ (CH ₃)CHCH ₂ -CH ₂	C ₂ H ₅
406	CH ₃ CH ₂ CH ₂ (CH ₃)CH-(CH ₃)-CH	C ₂ H ₅
407	CH ₃ CH ₂ (CH ₃)CHCH ₂ -(CH ₃)-CH	C ₂ H ₅
408	HOCH ₂ CH ₂	C ₂ H ₅
409	CH ₃ OCH ₂ CH ₂	C ₂ H ₅

Cmpd No	R ³	R ⁴
410	CH ₃ OCH ₂ (CH ₃)CH	C ₂ H ₅
411	CH ₃ OCH ₂ (CF ₃)CH	C ₂ H ₅
412	CH ₃ OCH ₂ (CH ₃) ₂ C	C ₂ H ₅
413	CH ₃ O(CH ₃)CHCH ₂	C ₂ H ₅
414	CH ₃ O(CH ₃)CH(CH ₃)CH	C ₂ H ₅
415	HC≡CCH ₂	C ₂ H ₅
416	CH ₃ C≡CCH ₂	C ₂ H ₅
417	HC≡CCH ₂ CH ₂	C ₂ H ₅
418	HOCH ₂ CH ₂ CH ₂	C ₂ H ₅
419	CH ₃ OCH ₂ CH ₂ CH ₂	C ₂ H ₅
420	(CH ₃) ₃ SiCH ₂	C ₂ H ₅
421	C ₆ H ₅ CH ₂	C ₂ H ₅
422	C ₆ H ₅ (CH ₃)CH	C ₂ H ₅
423	4-F-C ₆ H ₄ CH ₂	C ₂ H ₅
424	4-Cl-C ₆ H ₄ CH ₂	C ₂ H ₅
425	4-F-C ₆ H ₅ (CH ₃)CH	C ₂ H ₅
426	4-Cl-C ₆ H ₅ (CH ₃)CH	C ₂ H ₅
427	C ₆ H ₅ CH ₂ CH ₂	C ₂ H ₅
428	4-F-C ₆ H ₅ CH ₂ CH ₂	C ₂ H ₅
429	1-piperidino	C ₂ H ₅
430	1-pyrrolidino	C ₂ H ₅
431	cyclo-C ₅ H ₉ CH ₂	C ₂ H ₅
432	Bicyclo[2.2.1]hept-2-yl	C ₂ H ₅
433	1-CH ₃ -cyclopropyl	C ₂ H ₅
434	cis-2-CH ₃ -cyclopropyl	C ₂ H ₅
435	trans-2-CH ₃ -cyclopropyl	C ₂ H ₅
436	2,2-(CH ₃) ₂ -cyclopropyl	C ₂ H ₅
437	1-CH ₃ -cyclobutyl	C ₂ H ₅
438	cis-2-CH ₃ -cyclobutyl	C ₂ H ₅
439	trans-2-CH ₃ -cyclobutyl	C ₂ H ₅
440	cis-3-CH ₃ -cyclobutyl	C ₂ H ₅
441	trans-3-CH ₃ -cyclobutyl	C ₂ H ₅
442	2,2-(CH ₃) ₂ -cyclobutyl	C ₂ H ₅
443	3,3-(CH ₃) ₂ -cyclobutyl	C ₂ H ₅
444	1-CH ₃ -cyclopentyl	C ₂ H ₅
445	cis-2-CH ₃ -cyclopentyl	C ₂ H ₅
446	trans-2-CH ₃ -cyclopentyl	C ₂ H ₅

Cmpd No	R ³	R ⁴
447	<i>cis</i> -3-CH ₃ -cyclopentyl	C ₂ H ₅
448	<i>trans</i> -3-CH ₃ -cyclopentyl	C ₂ H ₅
449	2,2-(CH ₃) ₂ -cyclopentyl	C ₂ H ₅
450	3,3-(CH ₃) ₂ -cyclopentyl	C ₂ H ₅
451	1-CH ₃ -cyclohexyl	C ₂ H ₅
452	<i>cis</i> -2-CH ₃ -cyclohexyl	C ₂ H ₅
453	<i>trans</i> -2-CH ₃ -cyclohexyl	C ₂ H ₅
454	<i>cis</i> -3-CH ₃ -cyclohexyl	C ₂ H ₅
355	<i>trans</i> -3-CH ₃ -cyclohexyl	C ₂ H ₅
456	2,2-(CH ₃) ₂ -cyclohexyl	C ₂ H ₅
457	3,3-(CH ₃) ₂ -cyclohexyl	C ₂ H ₅
458	<i>cis</i> -4-CH ₃ -cyclohexyl	C ₂ H ₅
459	<i>trans</i> -4-CH ₃ -cyclohexyl	C ₂ H ₅
460	4,4-(CH ₃) ₂ -cyclohexyl	C ₂ H ₅
461	4-(CH ₃) ₃ C-cyclohexyl	C ₂ H ₅
462	<i>n</i> -C ₃ H ₇	CF ₃ CH ₂
463	<i>i</i> -C ₃ H ₇	CF ₃ CH ₂
464	<i>n</i> -C ₄ H ₉	CF ₃ CH ₂
465	<i>t</i> -C ₄ H ₉	CF ₃ CH ₂
466	CH ₂ =CHCH ₂	CF ₃ CH ₂
467	CH ₂ =C(CH ₃)CH ₂	CF ₃ CH ₂
468	CF ₃ CH ₂	CF ₃ CH ₂
469	CF ₃ CH ₂ CH ₂	CF ₃ CH ₂
470	CF ₃ CH ₂ CH ₂ CH ₂	CF ₃ CH ₂
471	CF ₃ (CH ₃)CH	CF ₃ CH ₂
472	(S)-CF ₃ (CH ₃)CH	CF ₃ CH ₂
473	(R)-CF ₃ (CH ₃)CH	CF ₃ CH ₂
474	cyclo-C ₃ H ₅	CF ₃ CH ₂
475	cyclo-C ₄ H ₇	CF ₃ CH ₂
476	cyclo-C ₅ H ₉	CF ₃ CH ₂
477	cyclo-C ₆ H ₁₁	CF ₃ CH ₂
478	cyclo-C ₃ H ₅ CH ₂	CF ₃ CH ₂
479	cyclo-C ₄ H ₇ CH ₂	CF ₃ CH ₂
480	cyclo-C ₆ H ₁₁ CH ₂	CF ₃ CH ₂
481	CH ₃ CH ₂ (CH ₃)CH	CF ₃ CH ₂
482	(S)-CH ₃ CH ₂ (CH ₃)CH	CF ₃ CH ₂
483	(R)-CH ₃ CH ₂ (CH ₃)CH	CF ₃ CH ₂

Cmpd No	R ³	R ⁴
484	cyclo-C ₇ H ₁₃	CF ₃ CH ₂
485	CH ₂ =C(CH ₃)CH ₂	CF ₃ CH ₂
486	CF ₃ CH ₂	CF ₃ CH ₂
487	4- <i>t</i> -C ₄ H ₉ -C ₆ H ₄ NH	CF ₃ CH ₂
488	4-F-C ₆ H ₄ NH	CF ₃ CH ₂
489	C ₆ H ₅ NH	CF ₃ CH ₂
490	4-CH ₃ -C ₆ H ₄ NH	CF ₃ CH ₂
491	4-Br-C ₆ H ₄ NH	CF ₃ CH ₂
492	2-F-C ₆ H ₄ NH	CF ₃ CH ₂
493	3,4-Cl ₂ -C ₆ H ₃ NH	CF ₃ CH ₂
494	3-CF ₃ -C ₆ H ₄ NH	CF ₃ CH ₂
495	3,5-Cl ₂ -C ₆ H ₃ NH	CF ₃ CH ₂
496	4-CF ₃ O-C ₆ H ₅ NH	CF ₃ CH ₂
497	2-CF ₃ -C ₆ H ₄ NH	CF ₃ CH ₂
498	4-CF ₃ -C ₆ H ₄ NH	CF ₃ CH ₂
499	2-Br-C ₆ H ₄ NH	CF ₃ CH ₂
500	2-Cl-C ₆ H ₄ NH	CF ₃ CH ₂
501	2-CH ₃ -4-Cl-C ₆ H ₃ NH	CF ₃ CH ₂
502	2-CH ₃ -5-F-C ₆ H ₃ NH	CF ₃ CH ₂
503	3-Cl-C ₆ H ₄ NH	CF ₃ CH ₂
504	(CH ₃) ₂ CHCH ₂	CF ₃ CH ₂
505	(CH ₃) ₃ CCH ₂	CF ₃ CH ₂
506	(CH ₃) ₃ C(CH ₃)CH	CF ₃ CH ₂
507	CH ₃ CH ₂ (CH ₃) ₂ C	CF ₃ CH ₂
508	CH ₃ CH ₂ (CF ₃)CH	CF ₃ CH ₂
509	(S)-CH ₃ CH ₂ (CF ₃)CH	CF ₃ CH ₂
510	(R)-CH ₃ CH ₂ (CF ₃)CH	CF ₃ CH ₂
511	CH ₃ CH ₂ (CH ₃ CH ₂)CH	CF ₃ CH ₂
512	(CH ₃) ₂ CH(CH ₃ CH ₂)CH	CF ₃ CH ₂
513	(CH ₃) ₂ CH(CH ₃)CH	CF ₃ CH ₂
514	(CH ₃) ₂ CH(CF ₃)CH	CF ₃ CH ₂
515	(S)-(CH ₃) ₂ CH(CF ₃)CH	CF ₃ CH ₂
516	(R)-(CH ₃) ₂ CH(CF ₃)CH	CF ₃ CH ₂
517	HC=C(CH ₃)CH ₂	CF ₃ CH ₂
518	CH ₂ =CH(CH ₃ CH ₂)CH	CF ₃ CH ₂
520	CH ₃ CH ₂ CH ₂ (CH ₃)CH	CF ₃ CH ₂
521	CH ₃ CH ₂ CH ₂ (CF ₃)CH	CF ₃ CH ₂

Cmpd No	R ³	R ⁴
522	(S)-CH ₃ CH ₂ CH ₂ (CF ₃)CH	CF ₃ CH ₂
523	(R)-CH ₃ CH ₂ CH ₂ (CF ₃)CH	CF ₃ CH ₂
524	CH ₃ CH ₂ CH ₂ (CH ₃) ₂ C	CF ₃ CH ₂
525	CH ₃ CH ₂ (CH ₃)CHCH ₂	CF ₃ CH ₂
526	(CH ₃) ₂ CHCH ₂ CH ₂	CF ₃ CH ₂
527	(CH ₃) ₃ CCH ₂ CH ₂	CF ₃ CH ₂
528	CH ₃ CH ₂ (CH ₃)CH(CH ₃)-CH	CF ₃ CH ₂
529	CH ₃ CH ₂ (CH ₃)CH(CF ₃)-CH	CF ₃ CH ₂
530	(S)-CH ₃ CH ₂ (CH ₃)CH-(CF ₃)-CH	CF ₃ CH ₂
531	(R)-CH ₃ CH ₂ (CH ₃)CH-(CF ₃)-CH	CF ₃ CH ₂
532	CH ₃ (CH ₃)CHCH ₂ (CH ₃)-CH	CF ₃ CH ₂
533	CH ₃ (CH ₃)CHCH ₂ (CF ₃)-CH	CF ₃ CH ₂
534	(S)-CH ₃ (CH ₃)CHCH ₂ -(CF ₃)CH	CF ₃ CH ₂
535	(R)-CH ₃ (CH ₃)CHCH ₂ -(CF ₃)CH	CF ₃ CH ₂
536	(CH ₃) ₂ CH(CH ₃)CH-(CH ₃)CH ₂	CF ₃ CH ₂
537	(CH ₃) ₃ CCH ₂ (CH ₃)CH	CF ₃ CH ₂
538	E-CH ₃ CH=CH(CH ₃)CH	CF ₃ CH ₂
539	E-CH ₃ CH=CH(CH ₃ CH ₂)-CH	CF ₃ CH ₂
540	CH ₃ CH ₂ CH ₂ (CH ₃ CH ₂)-CH	CF ₃ CH ₂
541	CH ₃ CH ₂ (CH ₃ CH ₂)CH-CH ₂	CF ₃ CH ₂
542	CF ₂ =CFCH ₂ CH ₂	CF ₃ CH ₂
543	CF ₃ CH ₂ (CH ₃)CHCH ₂	CF ₃ CH ₂
544	CF ₃ CF ₂ CH ₂ CH ₂	CF ₃ CH ₂
545	CF ₃ CF ₂ CF ₂ CH ₂	CF ₃ CH ₂
546	CF ₂ =C(CH ₃)CH ₂ CH ₂	CF ₃ CH ₂
547	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂	CF ₃ CH ₂
548	CH ₃ CH ₂ CH ₂ CH ₂ (CH ₃)-CH	CF ₃ CH ₂
549	CH ₃ CH ₂ CH ₂ (CH ₃)CH-CH ₂	CF ₃ CH ₂
550	CH ₃ CH ₂ (CH ₃)CHCH ₂ -CH ₂	CF ₃ CH ₂
551	CH ₃ CH ₂ CH ₂ (CH ₃)CH-(CH ₃)CH	CF ₃ CH ₂
552	CH ₃ CH ₂ (CH ₃)CHCH ₂ -(CH ₃)CH	CF ₃ CH ₂

Cmpd No	R ³	R ⁴
553	HOCH ₂ CH ₂	CF ₃ CH ₂
554	CH ₃ OCH ₂ CH ₂	CF ₃ CH ₂
555	CH ₃ OCH ₂ (CH ₃)CH	CF ₃ CH ₂
556	CH ₃ OCH ₂ (CF ₃)CH	CF ₃ CH ₂
557	CH ₃ OCH ₂ (CH ₃) ₂ C	CF ₃ CH ₂
558	CH ₃ O(CH ₃)CHCH ₂	CF ₃ CH ₂
559	CH ₃ O(CH ₃)CH(CH ₃)CH	CF ₃ CH ₂
560	HC≡CCH ₂	CF ₃ CH ₂
561	CH ₃ C≡CCH ₂	CF ₃ CH ₂
562	HC≡CCH ₂ CH ₂	CF ₃ CH ₂
563	HOCH ₂ CH ₂ CH ₂	CF ₃ CH ₂
564	CH ₃ OCH ₂ CH ₂ CH ₂	CF ₃ CH ₂
565	(CH ₃) ₃ SiCH ₂	CF ₃ CH ₂
566	C ₆ H ₅ CH ₂	CF ₃ CH ₂
567	C ₆ H ₅ (CH ₃)CH	CF ₃ CH ₂
568	4-F-C ₆ H ₄ CH ₂	CF ₃ CH ₂
569	4-Cl-C ₆ H ₄ CH ₂	CF ₃ CH ₂
570	4-F-C ₆ H ₅ (CH ₃)CH	CF ₃ CH ₂
571	4-Cl-C ₆ H ₅ (CH ₃)CH	CF ₃ CH ₂
572	C ₆ H ₅ CH ₂ CH ₂	CF ₃ CH ₂
573	4-F-C ₆ H ₅ CH ₂ CH ₂	CF ₃ CH ₂
574	1-piperidino	CF ₃ CH ₂
575	1-pyrrolidino	CF ₃ CH ₂
576	cyclo-C ₅ H ₉ CH ₂	CF ₃ CH ₂
577	bicyclo[2.2.1]hept-2-yl	CF ₃ CH ₂
578	1-CH ₃ -cyclopropyl	CF ₃ CH ₂
579	cis-2-CH ₃ -cyclopropyl	CF ₃ CH ₂
580	trans-2-CH ₃ -cyclopropyl	CF ₃ CH ₂
581	2,2-(CH ₃) ₂ -cyclopropyl	CF ₃ CH ₂
582	1-CH ₃ -cyclobutyl	CF ₃ CH ₂
583	cis-2-CH ₃ -cyclobutyl	CF ₃ CH ₂
584	trans-2-CH ₃ -cyclobutyl	CF ₃ CH ₂
585	cis-3-CH ₃ -cyclobutyl	CF ₃ CH ₂
586	trans-3-CH ₃ -cyclobutyl	CF ₃ CH ₂
587	2,2-(CH ₃) ₂ -cyclobutyl	CF ₃ CH ₂
588	3,3-(CH ₃) ₂ -cyclobutyl	CF ₃ CH ₂
589	1-CH ₃ -cyclopentyl	CF ₃ CH ₂

Cmpd No	R ³	R ⁴
590	<i>cis</i> -2-CH ₃ -cyclopentyl	CF ₃ CH ₂
591	<i>trans</i> -2-CH ₃ -cyclopentyl	CF ₃ CH ₂
592	<i>cis</i> -3-CH ₃ -cyclopentyl	CF ₃ CH ₂
593	<i>trans</i> -3-CH ₃ -cyclopentyl	CF ₃ CH ₂
594	2,2-(CH ₃) ₂ -cyclopentyl	CF ₃ CH ₂
595	3,3-(CH ₃) ₂ -cyclopentyl	CF ₃ CH ₂
596	1-CH ₃ -cyclohexyl	CF ₃ CH ₂
597	<i>cis</i> -2-CH ₃ -cyclohexyl	CF ₃ CH ₂
598	<i>trans</i> -2-CH ₃ -cyclohexyl	CF ₃ CH ₂
599	<i>cis</i> -3-CH ₃ -cyclohexyl	CF ₃ CH ₂
600	<i>trans</i> -3-CH ₃ -cyclohexyl	CF ₃ CH ₂
601	2,2-(CH ₃) ₂ -cyclohexyl	CF ₃ CH ₂
602	3,3-(CH ₃) ₂ -cyclohexyl	CF ₃ CH ₂
603	<i>cis</i> -4-CH ₃ -cyclohexyl	CF ₃ CH ₂
604	<i>trans</i> -4-CH ₃ -cyclohexyl	CF ₃ CH ₂
605	4,4-(CH ₃) ₂ -cyclohexyl	CF ₃ CH ₂
606	4-(CH ₃) ₃ C-cyclohexyl	CF ₃ CH ₂
607	<i>cis</i> -1-CH ₃ -2-fluoro-cyclopropyl	H
608	<i>trans</i> -1-CH ₃ -2-fluoro-cyclopropyl	H
609	1-CH ₃ -2,2-difluoro-cyclopropyl	H
610	<i>cis</i> -1-CH ₃ -2-chloro-2-fluorocyclopropyl	H
611	<i>trans</i> -1-CH ₃ -2-chloro-2-fluorocyclopropyl	H
612	CH ₃ CO(CH ₃)CH	H
613	CH ₃ CH ₂ CO(CH ₃)CH	H
614	(CH ₃) ₂ CHCO(CH ₃)CH	H
615	(CH ₃) ₃ CCO(CH ₃)CH	H
616	CH ₃ CH ₂ CH ₂ CO(CH ₃)CH	H
617	CH ₃ CO(CF ₃)CH	H
618	CH ₃ CH ₂ CO(CF ₃)CH	H
619	CH ₃ CO(CH ₃) ₂ C	H
620	CH ₃ CH ₂ CO(CH ₃) ₂ C	H
621	<i>cis</i> -1-CH ₃ -2-fluoro-cyclopropyl	CH ₃
622	<i>trans</i> -1-CH ₃ -2-fluoro-cyclopropyl	CH ₃
623	1-CH ₃ -2,2-difluoro-cyclopropyl	CH ₃

Cmpd No	R ³	R ⁴
624	<i>cis</i> -1-CH ₃ -2-chloro-2-fluorocyclopropyl	CH ₃
625	<i>trans</i> -1-CH ₃ -2-chloro-2-fluorocyclopropyl	CH ₃
626	CH ₃ CO(CH ₃)CH	CH ₃
627	CH ₃ CH ₂ CO(CH ₃)CH	CH ₃
628	(CH ₃) ₂ CHCO(CH ₃)CH	CH ₃
629	(CH ₃) ₃ CCO(CH ₃)CH	CH ₃
630	CH ₃ CH ₂ CH ₂ CO(CH ₃)CH	CH ₃
631	CH ₃ CO(CF ₃)CH	CH ₃
632	CH ₃ CH ₂ CO(CF ₃)CH	CH ₃
633	CH ₃ CO(CH ₃) ₂ C	CH ₃
634	CH ₃ CH ₂ CO(CH ₃) ₂ C	CH ₃
635	<i>cis</i> -1-CH ₃ -2-fluoro-cyclopropyl	C ₂ H ₅
636	<i>trans</i> -1-CH ₃ -2-fluoro-cyclopropyl	C ₂ H ₅
637	1-CH ₃ -2,2-difluoro-cyclopropyl	C ₂ H ₅
638	<i>cis</i> -1-CH ₃ -2-chloro-2-fluorocyclopropyl	C ₂ H ₅
639	<i>trans</i> -1-CH ₃ -2-chloro-2-fluorocyclopropyl	C ₂ H ₅
640	CH ₃ CO(CH ₃)CH	C ₂ H ₅
641	CH ₃ CH ₂ CO(CH ₃)CH	C ₂ H ₅
642	(CH ₃) ₂ CHCO(CH ₃)CH	C ₂ H ₅
643	(CH ₃) ₃ CCO(CH ₃)CH	C ₂ H ₅
644	CH ₃ CH ₂ CH ₂ CO(CH ₃)CH	C ₂ H ₅
645	CH ₃ CO(CF ₃)CH	C ₂ H ₅
646	CH ₃ CH ₂ CO(CF ₃)CH	C ₂ H ₅
647	CH ₃ CO(CH ₃) ₂ C	C ₂ H ₅
648	CH ₃ CH ₂ CO(CH ₃) ₂ C	C ₂ H ₅
649	<i>cis</i> -1-CH ₃ -2-fluoro-cyclopropyl	CF ₃ CH ₂
650	<i>trans</i> -1-CH ₃ -2-fluoro-cyclopropyl	CF ₃ CH ₂
651	1-CH ₃ -2,2-difluoro-cyclopropyl	CF ₃ CH ₂
652	<i>cis</i> -1-CH ₃ -2-chloro-2-fluorocyclopropyl	CF ₃ CH ₂
653	<i>trans</i> -1-CH ₃ -2-chloro-2-fluorocyclopropyl	CF ₃ CH ₂
654	CH ₃ CO(CH ₃)CH	CF ₃ CH ₂
655	CH ₃ CH ₂ CO(CH ₃)CH	CF ₃ CH ₂
656	(CH ₃) ₂ CHCO(CH ₃)CH	CF ₃ CH ₂

Cmpd No	R ³	R ⁴
657	(CH ₃) ₃ CCO(CH ₃)CH	CF ₃ CH ₂
658	CH ₃ CH ₂ CH ₂ CO(CH ₃)CH	CF ₃ CH ₂
659	CH ₃ CO(CF ₃)CH	CF ₃ CH ₂

Cmpd No	R ³	R ⁴
660	CH ₃ CH ₂ CO(CF ₃)CH	CF ₃ CH ₂
661	CH ₃ CO(CH ₃) ₂ C	CF ₃ CH ₂
662	CH ₃ CH ₂ CO(CH ₃) ₂ C	CF ₃ CH ₂

Table 2

Table 2 consists of 662 compounds of the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2,5,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 2 is the same as compound 1 of Table 1 except that in compound 1 of Table 2, R¹ is 2,5,6-trifluorophenyl. Similarly, compounds 2 to 662 of Table 2 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 2, R¹ is 2,5,6-trifluorophenyl.

Table 3

Table 3 consists of 662 compounds of the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2,3,4,5,6-pentafluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 3 is the same as compound 1 of Table 1 except that in compound 1 of Table 3, R¹ is 2,3,4,5,6-pentafluorophenyl. Similarly, compounds 2 to 662 of Table 3 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 3, R¹ is 2,3,4,5,6-pentafluorophenyl.

Table 4

Table 4 consists of 662 compounds of the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2,6-difluoro-4-methoxyphenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 4 is the same as compound 1 of Table 1 except that in compound 1 of Table 4, R¹ is 2,6-difluoro-4-methoxyphenyl. Similarly, compounds 2 to 662 of Table 4 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 4, R¹ is 2,6-difluoro-4-methoxyphenyl.

Table 5

Table 5 consists of 662 compounds of the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2-fluoro-6-chlorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 5 is the same as compound 1 of Table 1 except that in compound 1 of Table 5, R¹ is 2-fluoro-6-chlorophenyl. Similarly, compounds 2 to 662 of Table 5 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 5, R¹ is 2-fluoro-6-chlorophenyl.

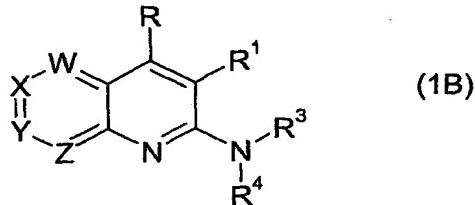
Table 6

Table 6 consists of 662 compounds of the general formula (1B), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2,4,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 6 is the same as compound 1 of Table 1 except that in compound 1 of Table 6, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 6 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 6, the compounds have the general formula (1B).

Table 7

Table 7 consists of 662 compounds of the general formula (1B), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2,5,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 7 is the same as compound 1 of Table 2 except that in compound 1 of Table 7, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 7 are the same as compounds 2 to 662 of Table 2 except that in the compounds of Table 7, the compounds have the general formula (1B).

Table 8

Table 8 consists of 662 compounds of the general formula (1B), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2,3,4,5,6-pentafluorophenyl, and the values of R³ and R⁴ are as listed in Table 3. Thus, compound 1 of Table 8 is the same as compound 1 of Table 3 except that in compound 1 of Table 8, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 8 are the same as compounds 2 to 662 of Table 3 except that in the compounds of Table 8, the compounds have the general formula (1B).

Table 9

Table 9 consists of 662 compounds of the general formula (1B), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2,6-difluoro-4-methoxyphenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 9 is the same as compound 1 of Table 4 except that in compound 1 of Table 9, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 9 are the same as compounds 2 to 662 of Table 4 except that in the compounds of Table 9, the compounds have the general formula (1B).

Table 10

Table 10 consists of 662 compounds of the general formula (1B), where W and Z are N, X and Y are CH, R is Cl, R¹ is 2-fluoro-6-chlorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 10 is the same as compound 1 of Table 5 except that in compound 1 of Table 10, the compound has the general formula (1B).

Similarly, compounds 2 to 662 of Table 10 are the same as compounds 2 to 662 of Table 5 except that in the compounds of Table 10, the compounds have the general formula (1B).

Table 11

Table 11 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2,4,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 11 is the same as compound 1 of Table 1 except that in compound 1 of Table 11, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 11 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 11, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 12

Table 12 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2,5,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 12 is the same as compound 1 of Table 2 except that in compound 1 of Table 12, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 12 are the same as compounds 2 to 662 of Table 2 except that in the compounds of Table 12, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 13

Table 13 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2,3,4,5,6-pentafluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 13 is the same as compound 1 of Table 3 except that in compound 1 of Table 13, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 13 are the same as compounds 2 to 662 of Table 3 except that in the compounds of Table 13, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 14

Table 14 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2,6-difluoro-4-methoxyphenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 14 is the same as compound 1 of Table 4 except that in compound 1 of Table 14, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 14 are the same as compounds 2 to 662 of Table 4 except that in the compounds of Table 14, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 15

Table 15 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2-fluoro-6-chlorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 15 is the same as compound 1 of Table 5 except that in compound 1 of Table 15, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 15 are the same as compounds 2 to 662 of Table 5 except that in the compounds of Table 15, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 16

Table 16 consists of 662 compounds of the general formula (1B), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2,4,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 16 is the same as compound 1 of Table 11 except that in compound 1 of Table 16, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 16 are the same as compounds 2 to 662 of Table 11 except that in the compounds of Table 16, the compounds have the general formula (1B).

Table 17

Table 17 consists of 662 compounds of the general formula (1B), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2,5,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 17 is the same as compound 1 of Table 12 except that in compound 1 of Table 17, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 17 are the same as compounds 2 to 662 of Table 12 except that in the compounds of Table 17, the compounds have the general formula (1B).

Table 18

Table 18 consists of 662 compounds of the general formula (1B), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2,3,4,5,6-pentafluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 18 is the same as compound 1 of

Table 13 except that in compound 1 of Table 18, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 18 are the same as compounds 2 to 662 of Table 13 except that in the compounds of Table 18, the compounds have the general formula (1B).

5 Table 19

Table 19 consists of 662 compounds of the general formula (1B), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2,6-difluoro-4-methoxyphenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 19 is the same as compound 1 of Table 14 except that in compound 1 of Table 19, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 19 are the same as compounds 2 to 662 of Table 14 except that in the compounds of Table 19, the compounds have the general formula (1B).

10 Table 20

Table 20 consists of 662 compounds of the general formula (1B), where W and X are N and Y and Z are CH, R is Cl, R¹ is 2-fluoro-6-chlorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 20 is the same as compound 1 of Table 15 except that in compound 1 of Table 20, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 20 are the same as compounds 2 to 662 of Table 15 except that in the compounds of Table 20, the compounds have the general formula (1B).

20 Table 21

Table 21 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2,4,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 21 is the same as compound 1 of Table 1 except that in compound 1 of Table 21, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 21 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 21, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 22

Table 22 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2,5,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 22 is the same as compound 1 of Table 2 except that in compound 1 of Table 22, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 22 are the same as

compounds 2 to 662 of Table 2 except that in the compounds of Table 22, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 23

Table 23 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2,3,4,5,6-pentafluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 23 is the same as compound 1 of Table 3 except that in compound 1 of Table 23, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 23 are the same as compounds 2 to 662 of Table 3 except that in the compounds of Table 23, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 24

Table 24 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2,6-difluoro-4-methoxyphenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 24 is the same as compound 1 of Table 4 except that in compound 1 of Table 24, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 24 are the same as compounds 2 to 662 of Table 4 except that in the compounds of Table 24, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 25

Table 25 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2-fluoro-6-chlorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 25 is the same as compound 1 of Table 5 except that in compound 1 of Table 25, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 25 are the same as compounds 2 to 662 of Table 5 except that in the compounds of Table 25, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 26

Table 26 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2,4,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 26 is the same as compound 1 of Table 1 except that in compound 1 of Table 26, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 26 are the same as

compounds 2 to 662 of Table 1 except that in the compounds of Table 26, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 27

Table 27 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2,5,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 27 is the same as compound 1 of Table 2 except that in compound 1 of Table 27, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 27 are the same as compounds 2 to 662 of Table 2 except that in the compounds of Table 27, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 28

Table 28 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2,3,4,5,6-pentafluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 28 is the same as compound 1 of Table 3 except that in compound 1 of Table 28, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 28 are the same as compounds 2 to 662 of Table 3 except that in the compounds of Table 28, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 29

Table 29 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2,6-difluoro-4-methoxyphenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 29 is the same as compound 1 of Table 4 except that in compound 1 of Table 29, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 29 are the same as compounds 2 to 662 of Table 4 except that in the compounds of Table 29, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 30

Table 30 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2-fluoro-6-chlorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 30 is the same as compound 1 of Table 5 except that in compound 1 of Table 30, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 30 are the same as

compounds 2 to 662 of Table 5 except that in the compounds of Table 30, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 31

Table 31 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 5 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 10 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 31 R¹ is 2,6-difluorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 32

Table 32 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 15 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 20 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 32 R¹ is 2-fluorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 33

Table 33 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 25 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 30 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 33 R¹ is 2,3,5,6-tetrafluorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 34

Table 34 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same

as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
5 compounds of Table 34 R¹ is 2-chloro-4,6-difluorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 35

Table 35 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
10 compounds of Table 35 R¹ is 2-chlorophenyl instead of 2-fluoro-6-chlorophenyl.
15 compounds of Table 35 R¹ is 2-chlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 36

Table 36 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
20 compounds of Table 36 R¹ is 2,6-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.
25 compounds of Table 36 R¹ is 2,6-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 37

Table 37 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
30 compounds of Table 37 R¹ is 2,4-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.
35 compounds of Table 37 R¹ is 2,4-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 38

Table 38 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 38 R¹ is 2,4,6-trichlorophenyl instead of 2-fluoro-6-chlorophenyl.

10 Table 39

Table 39 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 39 R¹ is 2,3,6-trichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 40

20 Table 40 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 40 R¹ is pentachlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 41

30 Table 41 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly

the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 41 R¹ is 2-fluoro-4,6-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.

5 Table 42

Table 42 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 42 R¹ is 4-fluoro-2,6-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.

10 Table 43

Table 43 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 43 R¹ is 2-bromophenyl instead of 2-fluoro-6-chlorophenyl.

15 Table 44

Table 44 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 44 R¹ is 2-fluoro-6-bromophenyl instead of 2-fluoro-6-chlorophenyl.

Table 45

Table 45 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 45 R¹ is 2-bromo-4,6-difluorophenyl instead of 2-fluoro-6-chlorophenyl.

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Table 46

Table 46 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 46 R¹ is 2-fluoro-6-methylphenyl instead of 2-fluoro-6-chlorophenyl.

15

Table 47

Table 47 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 47 R¹ is 2-chloro-6-methylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 48

30 Table 48 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the

same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 48 R¹ is 2-methoxyphenyl instead of 2-fluoro-6-chlorophenyl.

5 Table 49

Table 49 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 49 R¹ is 2,6-dimethoxyphenyl instead of 2-fluoro-6-chlorophenyl.

10 Table 50

15 Table 50 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 50 R¹ is 2-fluoro-6-methoxyphenyl instead of 2-fluoro-6-chlorophenyl.

20 Table 51

25 Table 51 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 51 R¹ is 2-trifluoromethylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 52

Table 52 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 52 R¹ is 2-fluoro-6-trifluoromethylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 53

Table 53 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 53 R¹ is 2,6-di-(trifluoromethyl)phenyl instead of 2-fluoro-6-chlorophenyl.

Table 54

Table 54 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 54 R¹ is 2-chloro-6-trifluoromethylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 55

Table 55 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as

compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 5 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 55 R¹ is 2,4-difluoro-6-trifluoromethylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 56

Table 56 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 10 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 15 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 56 R¹ is 2,4-difluoro-6-methoxyphenyl instead of 2-fluoro-6-chlorophenyl.

Table 57

Table 57 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 20 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 25 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 57 R¹ is 2,4-difluoro-6-methylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 58

Table 58 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 0 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly

the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 58 R¹ is 2,4-difluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 59

5 Table 59 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly 10 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 59 R¹ is 3,5-difluoropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 60

15 Table 60 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly 20 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 60 R¹ is tetrafluoropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 61

25 Table 61 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly 30 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 61 R¹ is 3-fluoropyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 62

Table 62 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as

compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 62 R¹ is 4-fluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 63

Table 63 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 63 R¹ is 3-fluoropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 64

Table 64 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 64 R¹ is 2-fluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 65

Table 65 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 65 R¹ is 2,4,6-trifluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 66

Table 66 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 66 R¹ is 3,5-difluoropyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

10 Table 67

Table 67 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 67 R¹ is 2,6-difluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 68

20 Table 68 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 68 R¹ is 2,4-difluoro-6-methoxypyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 69

30 Table 69 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the

same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 69 R¹ is 2-fluoro-4-chloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

5 Table 70

Table 70 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 70 R¹ is 3-fluoro-5-chloropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

10 Table 71

15 Table 71 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 71 R¹ is 2-chloro-4-fluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

20 Table 72

25 Table 72 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 72 R¹ is 2,4-dichloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 73

Table 73 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 73 R¹ is 3-chloropyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

10 Table 74

Table 74 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 74 R¹ is 4-chloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 75

20 Table 75 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 75 R¹ is 3-chloropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 76

30 Table 76 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly

the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 76 R¹ is 2-chloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 77

- 5 Table 77 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly
10 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 77 R¹ is 3-trifluoromethylpyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 78

- 15 Table 78 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly
20 the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 78 R¹ is 4-trifluoromethylpyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 79

- 25 Table 79 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
30 compounds of Table 79 R¹ is 3,5-dichloropyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 80

- Table 80 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as

compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 5 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 80 R¹ is 4,6-dichloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 81

Table 81 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as 10 compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the 15 compounds of Table 81 R¹ is 3-trifluoromethylpyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 82

Table 82 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as 20 compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 82 R¹ is 2-trifluoromethylpyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

25 Table 83

Table 83 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as 30 compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the

compounds of Table 83 R¹ is 2-fluoro-4-trifluoromethylpyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 84

Table 84 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 5 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly 10 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 84 R¹ is 3-fluoro-5-trifluoromethylpyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 85

Table 85 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 15 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly 20 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 85 R¹ is 4-fluoro-2-trifluoromethylpyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 86

Table 86 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as 25 compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly 30 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 86 R¹ is 2,6-dichloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 87

Table 87 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 87 R¹ is 3,5-dichloropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

10 Table 88

Table 88 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 88 R¹ is 3-chloro-6-trifluoromethylpyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

20 Table 89

Table 89 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 89 R¹ is 3-fluoro-6-trifluoromethylpyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

30 Table 90

Table 90 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same

as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
5 compounds of Table 90 R¹ is pyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 91

Table 91 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same
10 as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
compounds of Table 91 R¹ is pyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

15 Table 92

Table 92 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same
20 as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
compounds of Table 92 R¹ is pyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 93

25 Table 93 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly
30 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the
compounds of Table 93 R¹ is 3-fluorothien-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 94

Table 94 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 94 R¹ is 3-chlorothien-2-yl instead of 2-fluoro-6-chlorophenyl.

10 Table 95

Table 95 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 95 R¹ is 2,4-difluorothien-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 96

20 Table 96 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 96 R¹ is 2,4-dichlorothien-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 97

30 Table 97 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly

the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 97 R¹ is 2,4,5-trichlorothien-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 98

- 5 Table 98 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly 10 the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 98 R¹ is piperidino instead of 2-fluoro-6-chlorophenyl.

Table 99

- 15 Table 99 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 20 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 99 R¹ is 2-methylpiperidino instead of 2-fluoro-6-chlorophenyl.

Table 100

- 25 Table 100 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the 30 compounds of Table 100 R¹ is 2,6-dimethylpiperidino instead of 2-fluoro-6-chlorophenyl.

Table 101

- Table 101 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as

compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are 5 exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 101 R¹ is morpholino instead of 2-fluoro-6-chlorophenyl.

Table 102

Table 102 consists of 3972 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 663 to 1324 are exactly the same as 10 compounds 1 to 662 of Table 10 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 1987 to 2648 are exactly the same as compounds 1 to 662 of Table 20 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the 15 compounds of Table 102 R¹ is 2,6-dimethylmorpholino instead of 2-fluoro-6-chlorophenyl.

Table 103

Table 103 consists of 305,844 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 102 (thus, for example, compound 1 of 20 Table 103 is the same as compound 1 of Table 1, compound 663 of Table 103 is the same as compound 1 of Table 2, compound 19,861 of Table 103 is the same as compound 1 of Table 31, compound 305,844 of Table 103 is the same as compound 3,972 of Table 102) except that in all of the compounds of Table 103 R is F instead of Cl.

Table 104

Table 104 consists of 305,844 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 102 (thus, for example, compound 1 of 25 Table 104 is the same as compound 1 of Table 1, compound 663 of Table 104 is the same as compound 1 of Table 2, compound 19,861 of Table 104 is the same as compound 1 of Table 31, compound 305,844 of Table 104 is the same as compound 3,972 of Table 102) except that in all of the compounds of Table 104 R is Br instead of Cl.

30 Table 105

Table 105 consists of 305,844 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 102 (thus, for example, compound 1 of Table 105 is the same as compound 1 of Table 1, compound 663 of Table 105 is the same as

compound 1 of Table 2, compound 19,861 of Table 105 is the same as compound 1 of Table 31, compound 305,844 of Table 105 is the same as compound 3,972 of Table 102) except that in all of the compounds of Table 105 R is methyl instead of Cl.

Table 106

5 Table 106 consists of 305,844 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 102 (thus, for example, compound 1 of Table 106 is the same as compound 1 of Table 1, compound 663 of Table 106 is the same as compound 1 of Table 2, compound 19,861 of Table 106 is the same as compound 1 of Table 31, compound 305,844 of Table 106 is the same as compound 3,972 of Table 102) except
10 that in all of the compounds of Table 106 R is H instead of Cl.

Table 107

15 Table 107 consists of 305,844 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 102 (thus, for example, compound 1 of Table 107 is the same as compound 1 of Table 1, compound 663 of Table 107 is the same as compound 1 of Table 2, compound 19,861 of Table 107 is the same as compound 1 of Table 31, compound 305,844 of Table 107 is the same as compound 3,972 of Table 102) except
that in all of the compounds of Table 107 R is cyano instead of Cl.

Table 108

20 Table 108 consists of 305,844 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 102 (thus, for example, compound 1 of Table 108 is the same as compound 1 of Table 1, compound 663 of Table 108 is the same as compound 1 of Table 2, compound 19,861 of Table 108 is the same as compound 1 of Table 31, compound 305,844 of Table 108 is the same as compound 3,972 of Table 102) except
that in all of the compounds of Table 108 R is methoxy instead of Cl.

25 Table 109

Table 109 consists of 6620 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 10 (thus, for example, compound 1 of Table 109 is the same as compound 1 of Table 1, compound 663 of Table 109 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 109 X is CF
30 instead of CH.

Table 110

Table 110 consists of 6620 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 10 (thus, for example, compound 1 of Table

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110 is the same as compound 1 of Table 1, compound 663 of Table 110 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 110 X is CCl instead of CH.

Table 111

5 Table 111 consists of 6620 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 10 (thus, for example, compound 1 of Table 111 is the same as compound 1 of Table 1, compound 663 of Table 111 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 111 X is CBr instead of CH.

10 Table 112

Table 112 consists of 6620 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 10 (thus, for example, compound 1 of Table 112 is the same as compound 1 of Table 1, compound 663 of Table 112 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 112 X is CCH₃ instead of CH.

15

Table 113

Table 113 consists of 6620 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 10 (thus, for example, compound 1 of Table 113 is the same as compound 1 of Table 1, compound 663 of Table 113 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 113 Y is CF instead of CH.

20 Table 114

Table 114 consists of 6620 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 10 (thus, for example, compound 1 of Table 114 is the same as compound 1 of Table 1, compound 663 of Table 114 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 114 Y is CCl instead of CH.

25 Table 115

Table 115 consists of 6620 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 10 (thus, for example, compound 1 of Table 115 is the same as compound 1 of Table 1, compound 663 of Table 115 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 115 Y is CBr instead of CH.

30

Table 116

Table 116 consists of 6620 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 10 (thus, for example, compound 1 of Table 116 is the same as compound 1 of Table 1, compound 663 of Table 116 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 116 Y is CCH₃ instead of CH.

Table 117

Table 117 consists of 662 compounds of the general formula (1B), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2,4,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 117 is the same as compound 1 of Table 21 except that in compound 1 of Table 117, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 117 are the same as compounds 2 to 662 of Table 21 except that in the compounds of Table 117, the compounds have the general formula (1B).

Table 118

Table 118 consists of 662 compounds of the general formula (1B), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2,5,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 118 is the same as compound 1 of Table 22 except that in compound 1 of Table 118, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 118 are the same as compounds 2 to 662 of Table 22 except that in the compounds of Table 118, the compounds have the general formula (1B).

Table 119

Table 119 consists of 662 compounds of the general formula (1B), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2,3,4,5,6-pentafluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 119 is the same as compound 1 of Table 23 except that in compound 1 of Table 119, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 119 are the same as compounds 2 to 662 of Table 23 except that in the compounds of Table 119, the compounds have the general formula (1B).

Table 120

Table 120 consists of 662 compounds of the general formula (1B), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2,6-difluoro-4-methoxyphenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 120 is the same as compound 1 of Table 24 except that in compound 1 of Table 120, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 120 are the same as compounds 2 to 662 of

Table 24 except that in the compounds of Table 120, the compounds have the general formula (1B).

Table 121

Table 121 consists of 662 compounds of the general formula (1B), where W and Z are CH and X and Y are N, R is Cl, R¹ is 2-fluoro-6-chlorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 121 is the same as compound 1 of Table 25 except that in compound 1 of Table 121, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 121 are the same as compounds 2 to 662 of Table 25 except that in the compounds of Table 121, the compounds have the general formula (1B).

Table 122

Table 122 consists of 662 compounds of the general formula (1B), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2,4,6-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 122 is the same as compound 1 of Table 26 except that in compound 1 of Table 122, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 122 are the same as compounds 2 to 662 of Table 26 except that in the compounds of Table 122, the compounds have the general formula (1B).

Table 123

Table 123 consists of 662 compounds of the general formula (1B), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2,4,5-trifluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 123 is the same as compound 1 of Table 27 except that in compound 1 of Table 123, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 123 are the same as compounds 2 to 662 of Table 27 except that in the compounds of Table 123, the compounds have the general formula (1B).

Table 124

Table 124 consists of 662 compounds of the general formula (1B), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2,3,4,5,6-pentafluorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 124 is the same as compound 1 of Table 28 except that in compound 1 of Table 124, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 124 are the same as compounds 2 to 662 of Table 28 except that in the compounds of Table 124, the compounds have the general formula (1B).

Table 125

Table 125 consists of 662 compounds of the general formula (1B), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2,6-difluoro-4-methoxyphenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 125 is the same as compound 1 of Table 29 except that in compound 1 of Table 125, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 125 are the same as compounds 2 to 662 of Table 29 except that in the compounds of Table 125, the compounds have the general formula (1B).

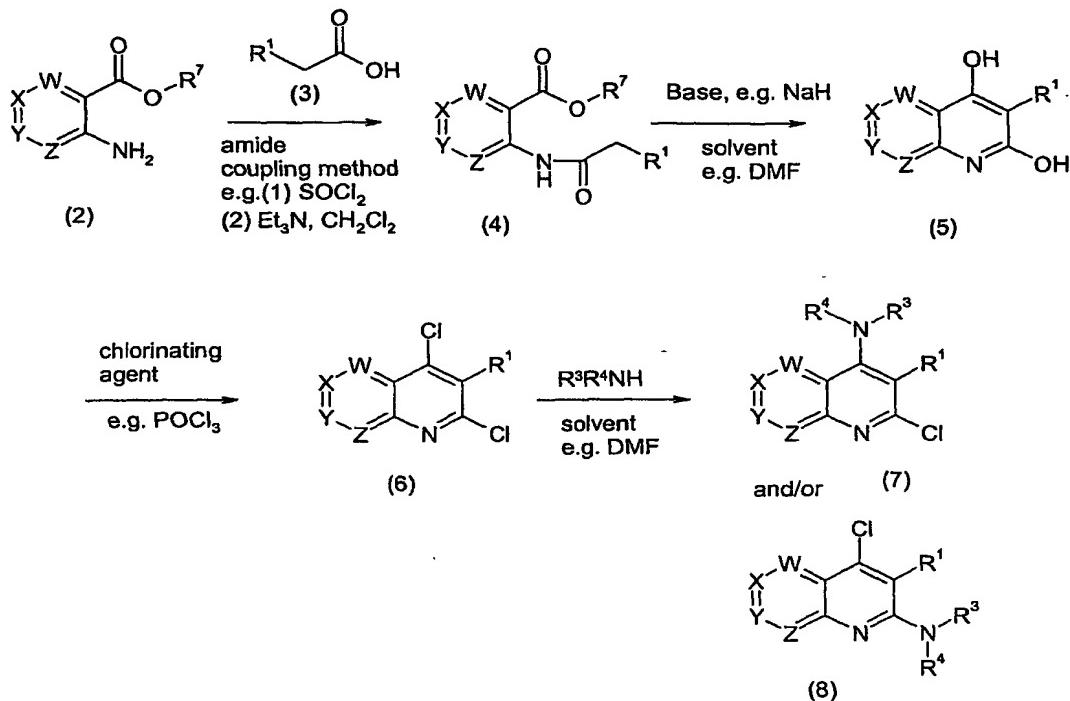
Table 126

Table 126 consists of 662 compounds of the general formula (1B), where W and X are CH and Y and Z are N, R is Cl, R¹ is 2-fluoro-6-chlorophenyl, and the values of R³ and R⁴ are as listed in Table 1. Thus, compound 1 of Table 126 is the same as compound 1 of Table 30 except that in compound 1 of Table 126, the compound has the general formula (1B). Similarly, compounds 2 to 662 of Table 126 are the same as compounds 2 to 662 of Table 30 except that in the compounds of Table 126, the compounds have the general formula (1B).

Table 127

Table 127 consists of 662 compounds of the general formula (1A), where W and Z are N and X and Y are CH, R is NR³R⁴, R¹ is 2,4,6-trifluorophenyl and the values of R³ and R⁴ are listed in Table 1. Thus, compound 1 of Table 127 is the same as compound 1 of Table 1 except that in compound 1 of Table 127, R is NR³R⁴. Similarly, compounds 2 to 662 of Table 127 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 127, R is NR³R⁴. It should be noted that in each compound there are the two NR³R⁴ groups, both of which are the same. In other words R³ and R⁴ in the NR³R⁴ group shown in formula (1A) and in the NR³R⁴ group that is R, have the same values. These are the values set out in Table 1.

Compounds of formula (7) or (8), which are examples of compounds of general formula (1) where one of R and R² is NR³R⁴, can be made as shown in Scheme 1, in which W, X, Y, Z, R¹, R³ and R⁴ have the meanings given above and R⁷ is C₁₋₄ alkyl.

Scheme 1

Compounds of general formula (4) can be prepared from compounds of general formula (2), which are either commercially available or made by methods known in the literature, by reaction with acids of general formula (3), using standard coupling methods, for example by conversion to the acid chloride using a chlorinating agent such as thionyl chloride, followed by reaction of the resultant acid chloride optionally in the presence of a base such as triethylamine, in a suitable solvent such as dichloromethane or toluene.

Compounds of general formula (5) can be prepared by treating compounds of general formula (4) with a base such as sodium hydride, optionally in the presence of a Lewis acid such as magnesium oxide, in a suitable solvent such as *N,N*-dimethylformamide (DMF) or toluene, at between room temperature and 150°C, but preferably at 60-90°C. Compounds of general formula (6) can be prepared by reaction of compounds of general formula (5) with a chlorination reagent such as phosphorus oxychloride, either neat or in a suitable solvent such as toluene, at between 50 and 150°C, but preferably between 80 and 110°C, or in a microwave reactor at between 150 and 300°C, but preferably between 200 and 250°C.

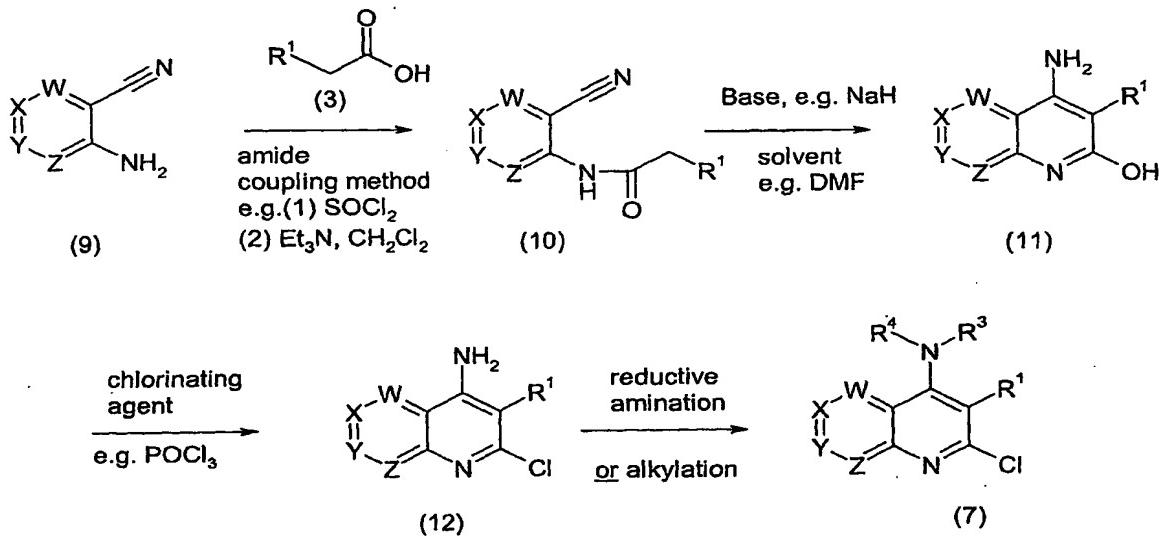
Compounds of formula (7) and (8) can be prepared by reaction of compounds of general formula (6) with an amine $\text{R}^3\text{R}^4\text{NH}$, either neat, or in a suitable solvent such as DMF,

between room temperature and 150°C, but preferably between 50 and 80°C. If compounds (7) and (8) are produced as a mixture they can be separated by suitable means such as crystallisation or chromatography under normal or reverse phase conditions.

Compounds of the general formulae (5), (6), (7) and (8) may be derivatised, via the chloro or hydroxy substituents, using routine chemical techniques to form other compounds of the general formula (1). Alternatively, other compounds of the general formula (1) may be prepared using a similar methodology to that described for preparing the compounds (5) to (8) and employing preparative techniques known from the chemical literature.

Compounds of formula (7) can also be made as shown in scheme 2.

10

Scheme 2

15

Compounds of general formula (10) can be prepared from compounds of general formula (9), which are either commercially available or made by methods known in the literature, by reaction with acids of general formula (3), using standard coupling methods, for example by conversion to the acid chloride using a chlorinating agent such as thionyl

chloride, followed by reaction of the resultant acid chloride optionally in the presence of a base such as triethylamine, in a suitable solvent such as dichloromethane or toluene.

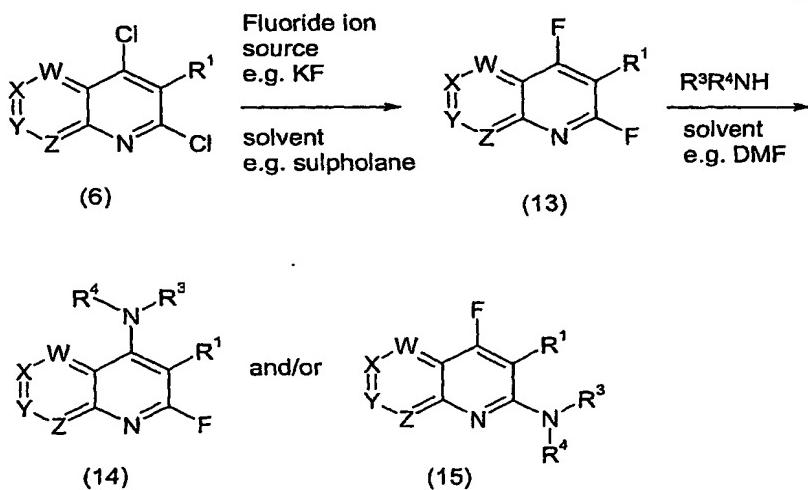
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Compounds of general formula (11) can be prepared by treating compounds of general formula (10) with a base such as sodium hydride, optionally in the presence of a Lewis acid such as magnesium oxide, in a suitable solvent such as *N,N*-dimethylformamide (DMF) or toluene, at between room temperature and 150°C, but preferably at 60-90°C. Compounds of

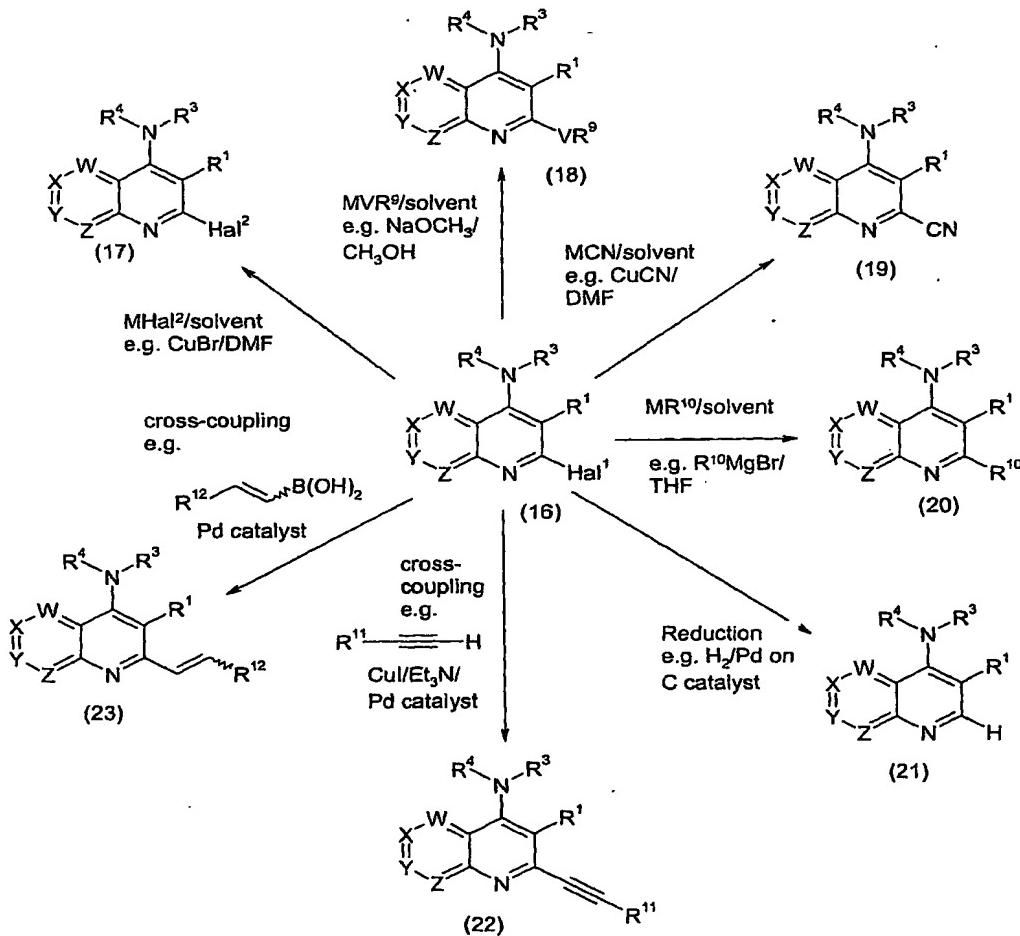
general formula (12) can be prepared by reaction of compounds of general formula (11) with a chlorination reagent such as phosphorus oxychloride, either neat or in a suitable solvent such as toluene, at between 50 and 150°C, but preferably between 80 and 110°C, or in a microwave reactor at between 150 and 300°C, but preferably between 200 and 250°C.

- 5 Compounds of formula (7) can be prepared from compounds of formula (12) by reductive amination, for example by reaction with a ketone or aldehyde in a suitable solvent such as ethanol or toluene, at between room temperature and reflux, optionally in the presence of an acid catalyst such as para-toluenesulphonic acid or a drying agent such as molecular sieves, followed by treatment with a suitable reducing agent such as sodium borohydride, at between
10 –20°C and 40°C, but preferably at room temperature. The aldehyde or ketone is chosen so that the desired groups R³ and R⁴ are formed after reduction of the product of reaction with the amine (12). For example if compounds of formula (12) are reacted with one equivalent of propionaldehyde and then sodium borohydride, compounds of formula (7) where R³ is *n*-propyl, and R⁴ is hydrogen are formed. If required, the reaction can be repeated with a
15 different aldehyde or ketone. For example, if acetone is used for the second reaction, then compounds of formula (7) where R³ is *n*-propyl and R⁴ is *iso*-propyl, are formed.
Alternatively compounds of formula (7) can be formed from compounds of formula (12) by alkylation with a group R³LG, by treatment with a suitable base such as sodium hydride in a solvent such as DMF, or a base such as potassium carbonate in a solvent such as acetone or
20 DMF, at between –78°C and 100°C, but preferably between room temperature and 60°C, followed by treatment with R⁴LG in a second step under the same conditions if required.

Scheme 3

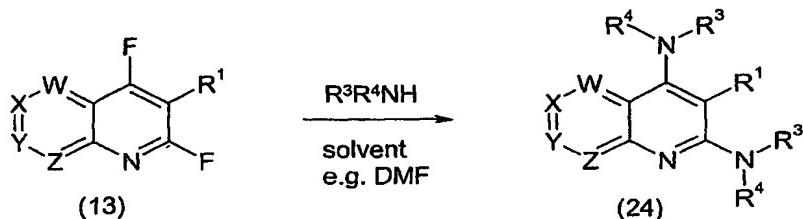


Compounds of formula (13) can be prepared as shown in Scheme 3 from compounds of formula (6) by reaction with a source of fluoride ion, such as potassium fluoride, in a suitable solvent such as sulpholane, at a temperature between 50°C and 200°C, but preferably at 80-150°C. Compounds of formula (14) and/or compounds of formula (15) can be prepared 5 from difluoro compounds of formula (13) by reaction with an amine of formula R³R⁴NH in a suitable solvent such as DMF or CH₂Cl₂, at a temperature of 0°C-100°C, but preferably at room temperature.

Scheme 4

Compounds of general formula (16), where Hal¹ is chlorine or fluorine, can be 0 converted into compounds of formula (17), (18), (19), (20), (21), (22) or (23) as shown in Scheme 4. Compounds of general formula (17) where Hal² is bromine or iodine can be formed by reacting compounds of general formula (16) with a metal halide, for example cuprous bromide, in a suitable solvent, for example DMF, at between room temperature and

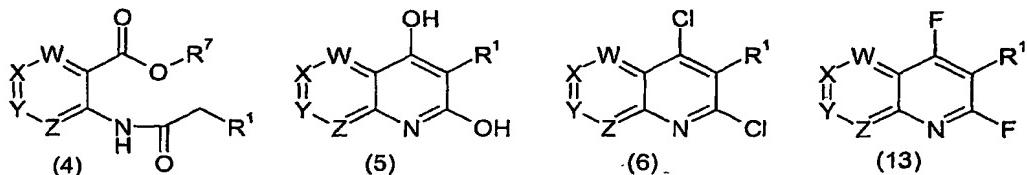
155°C, but preferably between 70°C and 155°C. Compounds of general formula (18) where V is oxygen or sulphur and R⁹ is C₁₋₈ alkyl, can be formed by reacting compounds of general formula (16) with a metal alkoxide or thioalkoxide MVR⁹ in a suitable solvent, for example sodium methoxide in methanol, at room temperature to 65°C. Compounds of general formula 5 (19) can be formed by reacting compounds of general formula (16) with a metal cyanide in a suitable solvent, for example cuprous cyanide in DMF, at between room temperature and 155°C but preferably between 50°C and 155°C. Compounds of general formula (20) where R¹⁰ is C₁₋₈ alkyl, can be formed by reacting compounds of general formula (16) with an alkyl metal derivative in a suitable solvent, for example methyl magnesium bromide in THF, 10 optionally in the presence of catalyst such as cuprous bromide or Pd(Ph)₄, between -40°C and 50°C. Compounds of general formula (21) can be formed by reduction of compounds of general formula (16), where Hal¹ is chlorine, for example by hydrogenolysis with hydrogen gas and a metal catalyst such as palladium on carbon in a suitable solvent such as ethanol, at room temperature. Compounds of general formula (22) where R¹¹ is hydrogen or C₁₋₆ alkyl, 15 can be formed by reaction of compounds of general formula (16) with an alkyl acetylene under the Sonogashira conditions, for example with 1-propyne in triethylamine in the presence of a cuprous salt such as cuprous iodide and a palladium catalyst such as Pd(Ph)₄, between room temperature and 70°C. Compounds of general formula (23) where R¹² is hydrogen or C₁₋₆ alkyl, can be formed by reaction of compounds of general formula (16) 20 with an alkenyl metal derivative in a suitable solvent, such as ethenylboronic acid in THF, in the presence of a palladium catalyst such as Pd(Ph)₄ and a base such as caesium carbonate, between room temperature and 65°C.

Scheme 5

In Scheme 5 compounds of general formula (24), where the two R³R⁴N groups are 25 identical, can be made from compounds of general formula (13) by reaction with a large excess of amine R³R⁴NH in a suitable solvent such as DMF, at a temperature between 0°C and 150°C, but preferably between room temperature and 100°C

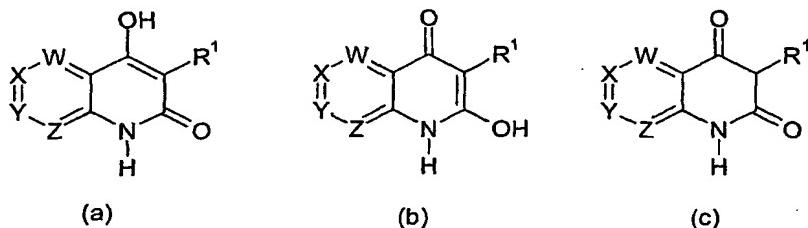
Further assistance in the preparation of the compounds of formula (1) may be derived from the following publications: Emilio, Toja, et. al., *J. Heterocyclic Chem.*, 23, 1955 (1986), H. Schäfer, et. al., *J. f. prakt. Chemie*, 321(4), 695 (1970) and H. Bredereck et. al., *Chem. Ber.* 96, 1868-1872 (1993).

- 5 The intermediate chemicals having the general formulae (4), (5), (6) and (13):



wherein W, X, Y, Z, R¹ and R⁷ are as defined above, are believed to be novel compounds and form a further part of this invention.

- It should be noted that the intermediate of general formula (5) may exist in the tautomeric forms (a), (b) and (c) as well as in the form shown in formula (5):



The invention as defined by the general formula (5) embraces all such tautomers.

- Of particular interest are the intermediates listed in Tables 128 to 132 below. In Table 128 the compounds have the general formula (4) where R⁷ is methyl and W, X, Y, Z and R¹ have the values shown in the table.

Table 128

Cmpd No.	R ¹	W	X	Y	Z
1	2,4,6-trifluorophenyl	N	CH	CH	N
2	2,5,6-trifluorophenyl	N	CH	CH	N
3	2,3,4,5,6-pentafluorophenyl	N	CH	CH	N
4	2,3,5,6-tetrafluorophenyl	N	CH	CH	N
5	2,6-difluoro-4-methoxyphenyl	N	CH	CH	N
6	2-fluoro-6-chlorophenyl	N	CH	CH	N
7	2,6-difluorophenyl	N	CH	CH	N

8	2,3,5,6-tetrafluorophenyl	N	CH	CH	N
9	2-fluorophenyl	N	CH	CH	N
10	2-chlorophenyl	N	CH	CH	N
11	2-bromophenyl	N	CH	CH	N
12	2,4-dichlorophenyl	N	CH	CH	N
13	2,4,6-trifluorophenyl	N	N	CH	CH
14	2,5,6-trifluorophenyl	N	N	CH	CH
15	2,3,4,5,6-pentafluorophenyl	N	N	CH	CH
16	2,3,5,6-tetrafluorophenyl	N	N	CH	CH
17	2,6-difluoro-4-methoxyphenyl	N	N	CH	CH
18	2-fluoro-6-chlorophenyl	N	N	CH	CH
19	2,6-difluorophenyl	N	N	CH	CH
20	2,3,5,6-tetrafluorophenyl	N	N	CH	CH
21	2-fluorophenyl	N	N	CH	CH
22	2-chlorophenyl	N	N	CH	CH
23	2-bromophenyl	N	N	CH	CH
24	2,4-dichlorophenyl	N	N	CH	CH
25	2,4,6-trifluorophenyl	CH	N	N	CH
26	2,5,6-trifluorophenyl	CH	N	N	CH
27	2,3,4,5,6-pentafluorophenyl	CH	N	N	CH
28	2,3,5,6-tetrafluorophenyl	CH	N	N	CH
29	2,6-difluoro-4-methoxyphenyl	CH	N	N	CH
30	2-fluoro-6-chlorophenyl	CH	N	N	CH
31	2,6-difluorophenyl	CH	N	N	CH
32	2,3,5,6-tetrafluorophenyl	CH	N	N	CH
33	2-fluorophenyl	CH	N	N	CH
34	2-chlorophenyl	CH	N	N	CH
35	2-bromophenyl	CH	N	N	CH
36	2,4-dichlorophenyl	CH	N	N	CH
37	2,4,6-trifluorophenyl	CH	CH	N	N
38	2,5,6-trifluorophenyl	CH	CH	N	N
39	2,3,4,5,6-pentafluorophenyl	CH	CH	N	N

40	2,3,5,6-tetrafluorophenyl	CH	CH	N	N
41	2,6-difluoro-4-methoxyphenyl	CH	CH	N	N
42	2-fluoro-6-chlorophenyl	CH	CH	N	N
43	2,6-difluorophenyl	CH	CH	N	N
44	2,3,5,6-tetrafluorophenyl	CH	CH	N	N
45	2-fluorophenyl	CH	CH	N	N
46	2-chlorophenyl	CH	CH	N	N
47	2-bromophenyl	CH	CH	N	N
48	2,4-dichlorophenyl	CH	CH	N	N

Table 129

Table 129 consists of 48 compounds of the general formula (5), where W, X, Y, Z and R¹ have the values given in Table 128. Thus, compound 1 of Table 129 has the same W, X, Y, Z and R¹ values as compound 1 of Table 128, etc.

Table 130

Table 130 consists of 48 compounds of the general formula (6), where W, X, Y, Z and R¹ have the values given in Table 128. Thus, compound 1 of Table 130 has the same W, X, Y, Z and R¹ values as compound 1 of Table 128, etc.

Table 131

Table 131 consists of 48 compounds of the general formula (13), where W, X, Y, Z and R¹ have the values given in Table 128. Thus, compound 1 of Table 131 has the same W, X, Y, Z and R¹ values as compound 1 of Table 128, etc.

Table 132

Table 132 consists of 48 compounds of the general formula (4), where W, X, Y, Z and R¹ have the values given in Table 128 and R⁷ is ethyl. Thus, compound 1 of Table 132 is the same as compound 1 of Table 128 except that in compound 1 of Table 132, R⁷ is ethyl instead of methyl. Similarly, compounds 2 to 48 of Table 132 are the same as compounds 2 to 48 of Table 128 except that in the compounds of Table 132, R⁷ is ethyl.

The compounds of formula (1) are active fungicides and may be used to control one or more of the following pathogens: *Pyricularia oryzae* (*Magnaporthe grisea*) on rice and wheat and other *Pyricularia* spp. on other hosts; *Puccinia triticina* (or *recondita*), *Puccinia striiformis* and other rusts on wheat, *Puccinia hordei*, *Puccinia striiformis* and other rusts on barley, and rusts on other hosts (for example turf, rye, coffee, pears, apples, peanuts, sugar

- beet, vegetables and ornamental plants); *Erysiphe cichoracearum* on cucurbits (for example melon); *Blumeria* (or *Erysiphe*) *graminis* (powdery mildew) on barley, wheat, rye and turf and other powdery mildews on various hosts, such as *Sphaerotheca macularis* on hops, *Sphaerotheca fusca* (*Sphaerotheca fuliginea*) on cucurbits (for example cucumber),
- 5 *Leveillula taurica* on tomatoes, aubergine and green pepper, *Podosphaera leucotricha* on apples and *Uncinula necator* on vines; *Cochliobolus* spp., *Helminthosporium* spp., *Drechslera* spp. (*Pyrenophora* spp.), *Rhynchosporium* spp., *Mycosphaerella graminicola* (*Septoria tritici*) and *Phaeosphaeria nodorum* (*Stagonospora nodorum* or *Septoria nodorum*), *Pseudocercospora herpotrichoides* and *Gaeumannomyces graminis* on cereals
- 10 (for example wheat, barley, rye), turf and other hosts; *Cercospora arachidicola* and *Cercosporidium personatum* on peanuts and other *Cercospora* spp. on other hosts, for example sugar beet, bananas, soya beans and rice; *Botrytis cinerea* (grey mould) on tomatoes, strawberries, vegetables, vines and other hosts and other *Botrytis* spp. on other hosts; *Alternaria* spp. on vegetables (for example carrots), oil-seed rape, apples, tomatoes, potatoes, cereals (for example wheat) and other hosts; *Venturia* spp. (including *Venturia inaequalis* (scab)) on apples, pears, stone fruit, tree nuts and other hosts; *Cladosporium* spp. on a range of hosts including cereals (for example wheat) and tomatoes; *Monilinia* spp. on stone fruit, tree nuts and other hosts; *Didymella* spp. on tomatoes, turf, wheat, cucurbits and other hosts; *Phoma* spp. on oil-seed rape, turf, rice, potatoes, wheat and other hosts;
- 15 20 *Aspergillus* spp. and *Aureobasidium* spp. on wheat, lumber and other hosts; *Ascochyta* spp. on peas, wheat, barley and other hosts; *Stemphylium* spp. (*Pleospora* spp.) on apples, pears, onions and other hosts; summer diseases (for example bitter rot (*Glomerella cingulata*), black rot or frogeye leaf spot (*Botryosphaeria obtusa*), Brooks fruit spot (*Mycosphaerella pomi*), Cedar apple rust (*Gymnosporangium juniperi-virginianae*), sooty blotch (*Gloeodes pomigena*), flyspeck (*Schizothyrium pomi*) and white rot (*Botryosphaeria dothidea*)) on apples and pears; *Plasmopara viticola* on vines; other downy mildews, such as *Bremia lactucae* on lettuce, *Peronospora* spp. on soybeans, tobacco, onions and other hosts, *Pseudoperonospora humuli* on hops and *Pseudoperonospora cubensis* on cucurbits; *Pythium* spp. (including *Pythium ultimum*) on turf and other hosts; *Phytophthora infestans* on potatoes and tomatoes and other *Phytophthora* spp. on vegetables, strawberries, avocado, pepper, ornamentals, tobacco, cocoa and other hosts; *Thanatephorus cucumeris* on rice and turf and other *Rhizoctonia* spp. on various hosts such as wheat and barley, peanuts, vegetables, cotton and turf; *Sclerotinia* spp. on turf, peanuts, potatoes, oil-seed rape and other hosts; *Sclerotium*

spp. on turf, peanuts and other hosts; *Gibberella fujikuroi* on rice; *Colletotrichum* spp. on a range of hosts including turf, coffee and vegetables; *Laetisaria fuciformis* on turf; *Mycosphaerella* spp. on bananas, peanuts, citrus, pecans, papaya and other hosts; *Diaporthe* spp. on citrus, soybean, melon, pears, lupin and other hosts; *Elsinoe* spp. on citrus, vines, olives, pecans, roses and other hosts; *Verticillium* spp. on a range of hosts including hops, potatoes and tomatoes; *Pyrenopeziza* spp. on oil-seed rape and other hosts; *Oncobasidium theobromae* on cocoa causing vascular streak dieback; *Fusarium* spp., *Typhula* spp., *Microdochium niveale*, *Ustilago* spp., *Urocystis* spp., *Tilletia* spp. and *Claviceps purpurea* on a variety of hosts but particularly wheat, barley, turf and maize; *Ramularia* spp. on sugar beet, barley and other hosts; post-harvest diseases particularly of fruit (for example *Penicillium digitatum*, *Penicillium italicum* and *Trichoderma viride* on oranges, *Colletotrichum musae* and *Gloeosporium musarum* on bananas and *Botrytis cinerea* on grapes); other pathogens on vines, notably *Eutypa lata*, *Guignardia bidwellii*, *Phellinus igniarus*, *Phomopsis viticola*, *Pseudopeziza tracheiphila* and *Stereum hirsutum*; other pathogens on trees (for example *Lophodermium sediticum*) or lumber, notably *Cephaloascus fragrans*, *Ceratocystis* spp., *Ophiostoma piceae*, *Penicillium* spp., *Trichoderma pseudokoningii*, *Trichoderma viride*, *Trichoderma harzianum*, *Aspergillus niger*, *Leptographium lindbergi* and *Aureobasidium pullulans*; and fungal vectors of viral diseases (for example *Polymyxa graminis* on cereals as the vector of barley yellow mosaic virus (BYMV) and *Polymyxa betae* on sugar beet as the vector of rhizomania).

A compound of formula (1) may move acropetally, basipetally or locally in plant tissue to be active against one or more fungi. Moreover, a compound of formula (1) may be volatile enough to be active in the vapour phase against one or more fungi on the plant.

The invention therefore provides a method of combating or controlling phytopathogenic fungi which comprises applying a fungicidally effective amount of a compound of formula (1), or a composition containing a compound of formula (1), to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or any other plant growth medium, e.g. nutrient solution.

The term "plant" as used herein includes seedlings, bushes and trees. Furthermore, the fungicidal method of the invention includes protectant, curative, systemic, eradicant and antifungal treatments.

The compounds of formula (1) are preferably used for agricultural, horticultural and turfgrass purposes in the form of a composition.

In order to apply a compound of formula (1) to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or any other growth medium, a compound of formula (1) is usually formulated into a composition which includes, in addition to the compound of formula (1), a suitable inert diluent or carrier and, optionally, a surface active agent (SFA).

- 5 SFAs are chemicals that are able to modify the properties of an interface (for example, liquid/solid, liquid/air or liquid/liquid interfaces) by lowering the interfacial tension and thereby leading to changes in other properties (for example dispersion, emulsification and wetting). It is preferred that all compositions (both solid and liquid formulations) comprise, by weight, 0.0001 to 95%, more preferably 1 to 85%, for example 5 to 60%, of a compound
10 of formula (1). The composition is generally used for the control of fungi such that a compound of formula (1) is applied at a rate of from 0.1g to 10kg per hectare, preferably from 1g to 6kg per hectare, more preferably from 1g to 1kg per hectare.

When used in a seed dressing, a compound of formula (1) is used at a rate of 0.0001g to 10g (for example 0.001g or 0.05g), preferably 0.005g to 10g, more preferably 0.005g to
15 4g, per kilogram of seed.

In another aspect the present invention provides a fungicidal composition comprising a fungicidally effective amount of a compound of formula (1) and a suitable carrier or diluent therefor.

In a still further aspect the invention provides a method of combating and controlling
20 fungi at a locus, which comprises treating the fungi, or the locus of the fungi with a fungicidally effective amount of a composition comprising a compound of formula (1).

The compositions can be chosen from a number of formulation types, including dustable powders (DP), soluble powders (SP), water soluble granules (SG), water dispersible granules (WG), wettable powders (WP), granules (GR) (slow or fast release), soluble
25 concentrates (SL), oil miscible liquids (OL), ultra low volume liquids (UL), emulsifiable concentrates (EC), dispersible concentrates (DC), emulsions (both oil in water (EW) and water in oil (EO)), micro-emulsions (ME), suspension concentrates (SC), aerosols, fogging/smoke formulations, capsule suspensions (CS) and seed treatment formulations. The formulation type chosen in any instance will depend upon the particular purpose envisaged
30 and the physical, chemical and biological properties of the compound of formula (1).

Dustable powders (DP) may be prepared by mixing a compound of formula (1) with one or more solid diluents (for example natural clays, kaolin, pyrophyllite, bentonite, alumina, montmorillonite, kieselguhr, chalk, diatomaceous earths, calcium phosphates,

calcium and magnesium carbonates, sulphur, lime, flours, talc and other organic and inorganic solid carriers) and mechanically grinding the mixture to a fine powder.

Soluble powders (SP) may be prepared by mixing a compound of formula (1) with one or more water-soluble inorganic salts (such as sodium bicarbonate, sodium carbonate or magnesium sulphate) or one or more water-soluble organic solids (such as a polysaccharide) and, optionally, one or more wetting agents, one or more dispersing agents or a mixture of said agents to improve water dispersibility/solubility. The mixture is then ground to a fine powder. Similar compositions may also be granulated to form water soluble granules (SG).

Wettable powders (WP) may be prepared by mixing a compound of formula (1) with one or more solid diluents or carriers, one or more wetting agents and, preferably, one or more dispersing agents and, optionally, one or more suspending agents to facilitate the dispersion in liquids. The mixture is then ground to a fine powder. Similar compositions may also be granulated to form water dispersible granules (WG).

Granules (GR) may be formed either by granulating a mixture of a compound of formula (1) and one or more powdered solid diluents or carriers, or from pre-formed blank granules by absorbing a compound of formula (1) (or a solution thereof, in a suitable agent) in a porous granular material (such as pumice, attapulgite clays, fuller's earth, kieselguhr, diatomaceous earths or ground corn cobs) or by adsorbing a compound of formula (1) (or a solution thereof, in a suitable agent) on to a hard core material (such as sands, silicates, mineral carbonates, sulphates or phosphates) and drying if necessary. Agents which are commonly used to aid absorption or adsorption include solvents (such as aliphatic and aromatic petroleum solvents, alcohols, ethers, ketones and esters) and sticking agents (such as polyvinyl acetates, polyvinyl alcohols, dextrins, sugars and vegetable oils). One or more other additives may also be included in granules (for example an emulsifying agent, wetting agent or dispersing agent).

Dispersible Concentrates (DC) may be prepared by dissolving a compound of formula (1) in water or an organic solvent, such as a ketone, alcohol or glycol ether. These solutions may contain a surface active agent (for example to improve water dilution or prevent crystallisation in a spray tank).

Emulsifiable concentrates (EC) or oil-in-water emulsions (EW) may be prepared by dissolving a compound of formula (1) in an organic solvent (optionally containing one or more wetting agents, one or more emulsifying agents or a mixture of said agents). Suitable organic solvents for use in ECs include aromatic hydrocarbons (such as alkylbenzenes or

alkylnaphthalenes, exemplified by SOLVESSO 100, SOLVESSO 150 and SOLVESSO 200; SOLVESSO is a Registered Trade Mark), ketones (such as cyclohexanone or methylcyclohexanone), alcohols (such as benzyl alcohol, furfuryl alcohol or butanol), *N*-alkylpyrrolidones (such as *N*-methylpyrrolidone or *N*-octylpyrrolidone), dimethyl amides of fatty acids (such as C₈-C₁₀ fatty acid dimethylamide) and chlorinated hydrocarbons. An EC product may spontaneously emulsify on addition to water, to produce an emulsion with sufficient stability to allow spray application through appropriate equipment. Preparation of an EW involves obtaining a compound of formula (1) either as a liquid (if it is not a liquid at room temperature, it may be melted at a reasonable temperature, typically below 70°C) or in solution (by dissolving it in an appropriate solvent) and then emulsifying the resultant liquid or solution into water containing one or more SFAs, under high shear, to produce an emulsion. Suitable solvents for use in EWs include vegetable oils, chlorinated hydrocarbons (such as chlorobenzenes), aromatic solvents (such as alkylbenzenes or alkylnaphthalenes) and other appropriate organic solvents that have a low solubility in water.

Microemulsions (ME) may be prepared by mixing water with a blend of one or more solvents with one or more SFAs, to produce spontaneously a thermodynamically stable isotropic liquid formulation. A compound of formula (1) is present initially in either the water or the solvent/SFA blend. Suitable solvents for use in MEs include those hereinbefore described for use in ECs or in EWs. An ME may be either an oil-in-water or a water-in-oil system (which system is present may be determined by conductivity measurements) and may be suitable for mixing water-soluble and oil-soluble pesticides in the same formulation. An ME is suitable for dilution into water, either remaining as a microemulsion or forming a conventional oil-in-water emulsion.

Suspension concentrates (SC) may comprise aqueous or non-aqueous suspensions of finely divided insoluble solid particles of a compound of formula (1). SCs may be prepared by ball or bead milling the solid compound of formula (1) in a suitable medium, optionally with one or more dispersing agents, to produce a fine particle suspension of the compound. One or more wetting agents may be included in the composition and a suspending agent may be included to reduce the rate at which the particles settle. Alternatively, a compound of formula (1) may be dry milled and added to water, containing agents hereinbefore described, to produce the desired end product.

Aerosol formulations comprise a compound of formula (1) and a suitable propellant (for example *n*-butane). A compound of formula (1) may also be dissolved or dispersed in a

suitable medium (for example water or a water miscible liquid, such as *n*-propanol) to provide compositions for use in non-pressurised, hand-actuated spray pumps.

A compound of formula (1) may be mixed in the dry state with a pyrotechnic mixture to form a composition suitable for generating, in an enclosed space, a smoke containing the compound.

Capsule suspensions (CS) may be prepared in a manner similar to the preparation of EW formulations but with an additional polymerisation stage such that an aqueous dispersion of oil droplets is obtained, in which each oil droplet is encapsulated by a polymeric shell and contains a compound of formula (1) and, optionally, a carrier or diluent therefor. The 10 polymeric shell may be produced by either an interfacial polycondensation reaction or by a coacervation procedure. The compositions may provide for controlled release of the compound of formula (1) and they may be used for seed treatment. A compound of formula (1) may also be formulated in a biodegradable polymeric matrix to provide a slow, controlled release of the compound.

15 A composition may include one or more additives to improve the biological performance of the composition (for example by improving wetting, retention or distribution on surfaces; resistance to rain on treated surfaces; or uptake or mobility of a compound of formula (1)). Such additives include surface active agents, spray additives based on oils, for example certain mineral oils or natural plant oils (such as soy bean and rape seed oil), and 20 blends of these with other bio-enhancing adjuvants (ingredients which may aid or modify the action of a compound of formula (1)).

A compound of formula (1) may also be formulated for use as a seed treatment, for example as a powder composition, including a powder for dry seed treatment (DS), a water soluble powder (SS) or a water dispersible powder for slurry treatment (WS), or as a liquid 25 composition, including a flowable concentrate (FS), a solution (LS) or a capsule suspension (CS). The preparations of DS, SS, WS, FS and LS compositions are very similar to those of, respectively, DP, SP, WP, SC and DC compositions described above. Compositions for treating seed may include an agent for assisting the adhesion of the composition to the seed (for example a mineral oil or a film-forming barrier).

30 Wetting agents, dispersing agents and emulsifying agents may be SFAs of the cationic, anionic, amphoteric or non-ionic type.

Suitable SFAs of the cationic type include quaternary ammonium compounds (for example cetyltrimethyl ammonium bromide), imidazolines and amine salts.

Suitable anionic SFAs include alkali metals salts of fatty acids, salts of aliphatic monoesters of sulphuric acid (for example sodium lauryl sulphate), salts of sulphonated aromatic compounds (for example sodium dodecylbenzenesulphonate, calcium dodecylbenzenesulphonate, butylnaphthalene sulphonate and mixtures of sodium di-isopropyl- and tri-isopropyl-naphthalene sulphonates), ether sulphates, alcohol ether sulphates (for example sodium laureth-3-sulphate), ether carboxylates (for example sodium laureth-3-carboxylate), phosphate esters (products from the reaction between one or more fatty alcohols and phosphoric acid (predominately mono-esters) or phosphorus pentoxide (predominately di-esters)), for example the reaction between lauryl alcohol and tetraphosphoric acid; additionally these products may be ethoxylated), sulphosuccinamates, paraffin or olefine sulphonates, taurates and lignosulphonates.

Suitable SFAs of the amphoteric type include betaines, propionates and glycimates.

Suitable SFAs of the non-ionic type include condensation products of alkylene oxides, such as ethylene oxide, propylene oxide, butylene oxide or mixtures thereof, with fatty alcohols (such as oleyl alcohol or cetyl alcohol) or with alkylphenols (such as octylphenol, nonylphenol or octylcresol); partial esters derived from long chain fatty acids or hexitol anhydrides; condensation products of said partial esters with ethylene oxide; block polymers (comprising ethylene oxide and propylene oxide); alkanolamides; simple esters (for example fatty acid polyethylene glycol esters); amine oxides (for example lauryl dimethyl amine oxide); and lecithins.

Suitable suspending agents include hydrophilic colloids (such as polysaccharides, polyvinylpyrrolidone or sodium carboxymethylcellulose) and swelling clays (such as bentonite or attapulgite).

A compound of formula (1) may be applied by any of the known means of applying fungicidal compounds. For example, it may be applied, formulated or unformulated, to any part of the plant, including the foliage, stems, branches or roots, to the seed before it is planted or to other media in which plants are growing or are to be planted (such as soil surrounding the roots, the soil generally, paddy water or hydroponic culture systems), directly or it may be sprayed on, dusted on, applied by dipping, applied as a cream or paste formulation, applied as a vapour or applied through distribution or incorporation of a composition (such as a granular composition or a composition packed in a water-soluble bag) in soil or an aqueous environment.

A compound of formula (1) may also be injected into plants or sprayed onto vegetation using electrodynamic spraying techniques or other low volume methods, or applied by land or aerial irrigation systems.

Compositions for use as aqueous preparations (aqueous solutions or dispersions) are generally supplied in the form of a concentrate containing a high proportion of the active ingredient, the concentrate being added to water before use. These concentrates, which may include DCs, SCs, ECs, EWs, MEs SGs, SPs, WPs, WG_s and CSs, are often required to withstand storage for prolonged periods and, after such storage, to be capable of addition to water to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional spray equipment. Such aqueous preparations may contain varying amounts of a compound of formula (1) (for example 0.0001 to 10%, by weight) depending upon the purpose for which they are to be used.

A compound of formula (1) may be used in mixtures with fertilisers (for example nitrogen-, potassium- or phosphorus-containing fertilisers). Suitable formulation types include granules of fertiliser. The mixtures suitably contain up to 25% by weight of the compound of formula (1).

The invention therefore also provides a fertiliser composition comprising a fertiliser and a compound of formula (1).

The compositions of this invention may contain other compounds having biological activity, for example micronutrients or compounds having similar or complementary fungicidal activity or which possess plant growth regulating, herbicidal, insecticidal, nematicidal or acaricidal activity.

By including another fungicide, the resulting composition may have a broader spectrum of activity or a greater level of intrinsic activity than the compound of formula (1) alone. Further the other fungicide may have a synergistic effect on the fungicidal activity of the compound of formula (1).

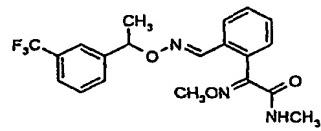
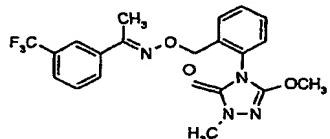
The compound of formula (1) may be the sole active ingredient of the composition or it may be admixed with one or more additional active ingredients such as a pesticide, fungicide, synergist, herbicide or plant growth regulator where appropriate. An additional active ingredient may: provide a composition having a broader spectrum of activity or increased persistence at a locus; synergise the activity or complement the activity (for example by increasing the speed of effect or overcoming repellency) of the compound of formula (1); or help to overcome or prevent the development of resistance to individual

components. The particular additional active ingredient will depend upon the intended utility of the composition.

- Examples of fungicidal compounds which may be included in the composition of the invention are AC 382042 (*N*-(1-cyano-1,2-dimethylpropyl)-2-(2,4-dichlorophenoxy) propionamide), acibenzolar-S-methyl, alanycarb, aldimorph, anilazine, azaconazole, azafenidin, azoxystrobin, benalaxyl, benomyl, benthiavalicarb, biloxazol, bitertanol, blasticidin S, boscalid (new name for nicobifen), bromuconazole, bupirimate, captafol, captan, carbendazim, carbendazim chlorhydrate, carboxin, carpropamid, carvone, CGA 41396, CGA 41397, chinomethionate, chlorbenzthiazole, chlorothalonil, chlorozolinate, clozylacon, copper containing compounds such as copper oxychloride, copper oxyquinolinate, copper sulphate, copper tallate, and Bordeaux mixture, cyamidazosulfamid, cyazofamid (IKF-916), cyflufenamid, cymoxanil, cyproconazole, cyprodinil, debacarb, di-2-pyridyl disulphide 1,1'-dioxide, dichlofuanid, diclocymet, diclomezine, dicloran, diethofencarb, difenoconazole, difenzoquat, diflumetorim, *O,O-di-iso-propyl-S-benzyl thiophosphate*, dimefluazole, dimetconazole, dimethirimol, dimethomorph, dimoxystrobin, diniconazole, dinocap, dithianon, dodecyl dimethyl ammonium chloride, dodemorph, dodine, doguadine, edifenphos, epoxiconazole, ethaboxam, ethirimol, ethyl (*Z*)-*N*-benzyl-*N*[(methyl(methylthioethylideneamino)oxycarbonyl)amino]thio)- β -alaninate, etridiazole, famoxadone, fenamidone, fenarimol, fenbuconazole, fenfuram, fenchexamid, fenoxanil (AC 382042), fenpiclonil, fenpropidin, fenpropimorph, fentin acetate, fentin hydroxide, ferbam, ferimzone, fluazinam, fludioxonil, flumetover, flumorph, fluoroimide, fluoxastrobin, fluquinconazole, flusilazole, flusulfamide, flutolanil, flutriafol, folpet, fosetyl-aluminium, fuberidazole, furalaxyd, furametpyr, guazatine, hexaconazole, hydroxyisoxazole, hymexazole, imazalil, imibenconazole, iminoctadine, iminoctadine triacetate, ipconazole, iprobenfos, iprodione, iprovalicarb, isopropanyl butyl carbamate, isoprothiolane, kasugamycin, kresoxim-methyl, LY186054, LY211795, LY 248908, mancozeb, manebe, mefenoxam, mepanipyrim, mepronil, metalaxyl, metalaxyl M, metconazole, metiram, metiram-zinc, metominostrobin, metrafenone, MON65500 (*N*-allyl-4,5-dimethyl-2-trimethylsilylthiophene-3-carboxamide), myclobutanil, NTN0301, neoasozin, nickel dimethyldithiocarbamate, nitrothale-isopropyl, nuarimol, ofurace, organomercury compounds, orysastrobin, oxadixyl, oxasulfuron, oxolinic acid, oxpoconazole, oxycarboxin, pefurazoate, penconazole, pencycuron, phenazin oxide, phosphorus acids, phthalide, picoxystrobin, polyoxin D, polyram, probenazole, prochloraz, procymidone, propamocarb, propamocarb hydrochloride, propiconazole, propineb, propionic

acid, proquinazid, prothioconazole, pyraclostrobin, pyrazophos, pyrifenoxy, pyrimethanil, pyroquilon, pyroxyfur, pyrrolnitrin, quaternary ammonium compounds, quinomethionate, quinoxyfen, quintozone, silthiofam (MON 65500), S-imazalil, simeconazole, sipconazole, sodium pentachlorophenate, spiroxamine, streptomycin, sulphur, tebuconazole, tecloftalam, 5 tecnazene, tetriconazole, thiabendazole, thifluzamide, 2-(thiocyanomethylthio)-benzothiazole, thiophanate-methyl, thiram, tiadinil, timibenconazole, tolclofos-methyl, tolylfuanid, triadimefon, triadimenol, triazbutil, triazoxide, tricyclazole, tridemorph, trifloxystrobin, triflumizole, triforine, triticonazole, validamycin A, vapam, vinclozolin, XRD-563, zineb, ziram, zoxamide and compounds of the formulae:

10



The compounds of formula (1) may be mixed with soil, peat or other rooting media for the protection of plants against seed-borne, soil-borne or foliar fungal diseases.

Some mixtures may comprise active ingredients, which have significantly different physical, chemical or biological properties such that they do not easily lend themselves to the same conventional formulation type. In these circumstances other formulation types may be prepared. For example, where one active ingredient is a water insoluble solid and the other a water insoluble liquid, it may nevertheless be possible to disperse each active ingredient in the same continuous aqueous phase by dispersing the solid active ingredient as a suspension (using a preparation analogous to that of an SC) but dispersing the liquid active ingredient as an emulsion (using a preparation analogous to that of an EW). The resultant composition is a suspoemulsion (SE) formulation.

The invention is illustrated by the following Examples in which the following abbreviations are used:

ml = millilitres

f = fine

g = grammes

THF = tetrahydrofuran

ppm = parts per million

DCM = dichloromethane

s = singlet

DMF = N, N-dimethylformamide

d = doublet

DMSO = dimethylsulphoxide

t = triplet

DMAP = 4-dimethylaminopyridine

q = quartet

NMR = nuclear magnetic resonance

m = multiplet

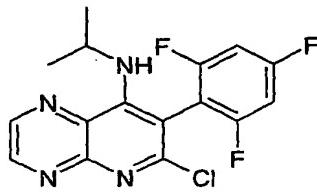
HPLC = high performance liquid

b = broad

chromatography

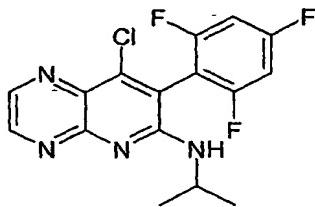
EXAMPLE 1

This Example illustrates the preparation of [6-chloro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-8-yl]-isopropylamine (Compound No. 3, Table 1) and [8-chloro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-6-yl]-isopropylamine (Compound No. 3, Table 6).



5

Compound No.3, Table 1



Compound No.3, Table 6

Step 1

Methyl 2-amino-3-pyrazine carboxylate (2.2 g) was dissolved in dry DCM (20 ml) to give a cloudy pale yellow solution, and pyridine (2 ml) in dry DCM (12 ml) was added. The stirred suspension was cooled in an ice bath, and 2,4,6-trifluorophenylacetyl chloride (3.0 g) in dry DCM (13 ml) was added dropwise. The reaction gradually became a deep orange, and then went clear. It was stirred for 6 hours and stood overnight. The reaction mixture was washed with water, brine, and then dilute hydrochloric acid, and the DCM layer was dried over magnesium sulphate. The solvent was evaporated to yield an orange solid which was triturated with ether, to give methyl 2-[2,4,6-trifluorophenylacetylamino]-3-pyrazine carboxylate as a yellow solid (1.5 g).

¹H NMR (CDCl₃) δ ppm: 4.03 (s,5H), 6.74 (t,2H), 8.43 (d,1H), 8.61 (d,1H) 10.9 (s,1H).

Step 2

The product of Step 1 (3.25 g) was dissolved in DMF (10ml) and added dropwise to a stirred suspension of sodium hydride (0.60 g of an 80% dispersion in mineral oil) in DMF (80 ml). There was an immediate reaction, and the mixture was stirred at room temperature for 2 hours, and at 80°C for 8 hours. The reaction mixture was cooled and evaporated to give a yellow solid (3 g), which was then acidified with dilute hydrochloric acid. The resultant white suspension was filtered and collected, washed with ether and dried to give 6,8-dihydroxy-7-(2,4,6-trifluorophenyl)pyrido[2,3-b]pyrazine (1.8 g).

¹H NMR (d⁶-DMSO) δ ppm: 7.25 (t,2H), 8.6 (fd,1H), 8.7 (fd,1H), 12.6 (s,1H).

Step 3

The product from Step 2 (0.90 g) was added portion-wise to phosphorus oxychloride (10 ml) with stirring. The reaction was exothermic. The mixture became brown with a fine suspension, and was then refluxed for 6 hours. Excess phosphorus oxychloride was

5 evaporated, the mixture was diluted with DCM, and then washed with water to give a black oil, which was purified by flash column chromatography on silica gel (40-60) eluting with diethyl ether, to give 6,8-dichloro-7-(2,4,6-trifluorophenyl)pyrido[2,3-b]pyrazine as a dark oil (0.40 g).

¹H NMR (CDCl₃) δ ppm: 6.9 (t,2H), 9.1(d,1H), 9.2 (d,1H).

10 Alternative procedure for Step 3

Phosphorus oxychloride (20.90 g) was added over 15 minutes to a suspension of the product from Step 2 (10.0 g), in 1,2-dichloroethane (80 ml) containing DMF (5.0 g) maintained at a temperature between 79°- 81°C. Stirring was continued at this temperature for 3 hours, and the reaction was then cooled. The mixture was poured carefully into

15 saturated sodium bicarbonate solution (500 ml) keeping the temperature below 30 °C. After stirring for 20 minutes the product was extracted with ethyl acetate, washed with water and brine and dried over sodium sulphate. The solvent was evaporated to yield a dark red oil, which was purified by flash chromatography eluting with cyclohexane:ethyl acetate, 4:1 to give 6,8-dichloro-7-(2,4,6-trifluorophenyl)pyrido[2,3-b]pyrazine as a light brown solid (7.5 g), m.p. 139-141 °C.

20 Step 4

The product from Step 3 (0.20 g), isopropylamine (1.0 ml) and *N*-ethyl-diisopropylamine (0.20 g) were refluxed in a sealed tube at 90°C for 17 hours. The dark coloured reaction mixture was evaporated to give an oil, which was purified by flash column chromatography on silica gel (40-60) in diethyl ether to give [8-chloro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-6-yl]-isopropylamine as a yellow solid (0.025 g).

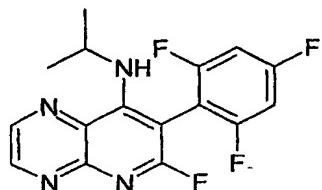
¹H NMR (CDCl₃) δ ppm: 1.25 (d,6H), 4.62 (bd,1H), 4.75 (m,1H), 6.67 (m,2H), 8.64 (d,1H), 8.85 (d,1H).

A fraction containing a mixture of isomers (0.080 g), was also obtained, and a portion of this 30 mixture (0.020g) was purified by reverse phase HPLC on a Kromasil 100-5C18 column, eluting with methanol:water (65:35) to give [6-chloro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-8-yl]-isopropylamine as a frothy solid (0.013 g).

¹H NMR (CDCl₃) δ ppm: 1.1 (d, 6H), 3.26 (m, 1H), 6.84 (m, 2H), 6.95 (bd, 1H), 8.67 (d, 1H), 9.0 (d, 1H).

EXAMPLE 2

This Example illustrates the preparation of [6-fluoro-7-(2,4,6-trifluorophenyl)-5 pyrido[2,3-b]pyrazin-8-yl]-isopropylamine (Compound No. 3, Table 103)



Step 1

6,8-Dichloro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazine (1.25 g) and potassium fluoride (0.66 g, spray dried) in dry sulpholane (5 ml) were heated to 130 °C for 16 hours.

10 The reaction mixture was poured into water and extracted with ethyl acetate. The extract was washed with water and brine and dried over sodium sulphate. After evaporation of the solvent, the remaining oil was purified by flash chromatography on silica gel eluting with cyclohexane:ethyl acetate, 3:1 to yield 6,8-disfluoro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]-pyrazine as a slightly brownish solid (0.79 g), m.p. 120-121 °C.

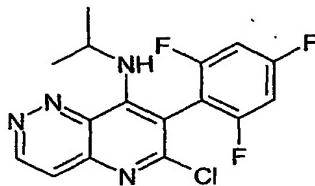
Step 2

The product from Step 1 (0.30 g) was added to a suspension of isopropylamine (0.090 g), potassium carbonate (0.21 g) and a catalytic amount of DMAP in DMF (3 ml), and the mixture was stirred at room temperature for 19 hours. After addition of ethyl acetate, the mixture was washed with water and brine, dried over sodium sulphate, filtered and the 20 solvent evaporated. The residue was purified by flash chromatography eluting with toluene:ethyl acetate, 9:1 to give [6-fluoro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-8-yl]-isopropylamine as a yellow powder (0.20 g), m.p. 127-128 °C.

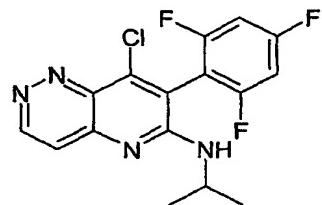
EXAMPLE 3

This Example illustrates the preparation of [6-chloro-7-(2,4,6-trifluorophenyl)-pyrido[3,2-

25 c]pyridazin-8-yl]-isopropylamine (Compound No. 3, Table 11) and [8-chloro-7-(2,4,6-trifluorophenyl)-pyrido[3,2-c]pyridazin-6-yl]-isopropylamine (Compound No. 3, Table 16).



Compound No. 3, Table 11



Compound No. 3, Table 16

Step 1

- A solution of 4-aminopyridazine-3-carbonitrile (0.248 g, prepared as in *J. Het. Chem.*(1970), 3, 467-473) in absolute ethanol (30 ml) was saturated with hydrogen chloride gas, the flask being cooled in an ice bath. The ice bath was then removed and the resulting solution was refluxed for 18 hours. It was then cooled, the solvent evaporated, and cold, saturated aqueous sodium bicarbonate was added. The aqueous phase was then extracted with DCM, the organic phases were combined, dried over magnesium sulphate, filtered and evaporated to give 4-aminopyridazine-3-carboxylic acid ethyl ester as a white solid (0.229g).
- The aqueous phase was evaporated, DCM was added, the organic phase was isolated, dried over magnesium sulphate, filtered and evaporated under *vacuo* to give further ester as a white solid (0.010 g), m.p. 149-150°C.

¹H NMR (CDCl₃) δ ppm: 1.48 (t,3H), 4.52 (q,2H), 6.73 (d,1H), 8.75 (d,1H).

Step 2

- A mixture of the product from Step 1 (0.239 g) and DMAP (0.175 g) in dry toluene (1 ml) was added to 2,4,6-trifluorophenylacetyl chloride (crude product from reaction of 0.275 g 2,4,6-trifluorophenylacetic acid and oxalyl chloride) and a few drops of DMF in toluene (1 ml) at room temperature, giving a thick yellow precipitate. The stirred suspension was heated for 3 hours at reflux, becoming dark brown/green with a green precipitate. It was left to stand overnight for 18 hours. The solid was collected and washed with diethyl ether. The dark green filtrate was evaporated to give a dark green liquid which was purified by flash column chromatography on silica gel (40-60) eluting with ethyl acetate to give 4-[2-(2,4,6-trifluorophenyl)-acetylamino]-pyridazine-3-carboxylic acid ethyl ester as green/yellow oil that solidified on standing (0.307 g).
- ¹H NMR (CDCl₃) δ ppm: 1.50 (t,3H), 3.87 (s,2H), 4.55 (q,2H), 6.77 (t,2H), 8.78 (d,1H), 9.15 (d,1H), 11.20 (bs,1H).

Step 3

The product from Step 2 (0.307 g) and potassium carbonate (0.25 g) were stirred in dry DMF (10 ml) at 110°C for 2 hours and then cooled and stood for 18 hours. The DMF was evaporated and the resulting brown solid was triturated with diethyl ether and the 5 organic phase decanted. The solid was dissolved in water then acidified with dilute hydrochloric acid to neutrality. Most of the aqueous phase was then evaporated, leading to precipitation of a black solid that was filtered, and the yellow/brown aqueous phase was evaporated to dryness, affording a residue that was dissolved in methanol, the insoluble inorganic salts were filtered and the organic phase was evaporated to dryness to give 7-
10 (2,4,6-trifluorophenyl)-5H-pyrido[3,2-c]pyridazine-6,8-dione as a light brown/beige solid (0.258 g).

¹H NMR (CD₃OD) δ ppm: 6.83 (2d,2H), 7.44 (d,1H), 9.00 (d,1H).

Step 4

Phosphorus oxychloride (0.048 ml) was added to the product from Step 3 (0.05 g) in 15 1,2-dichloroethane (2 ml) containing a catalytic amount of DMF. The suspension was stirred and refluxed for 1 hour and then stood for 18 hours, and then refluxed for a further hour and then allowed to cool. The excess phosphorus oxychloride was evaporated to give a brown oil, which was dissolved in DCM and washed with cold water. The organic layer was separated and dried over magnesium sulphate, filtered and evaporated to give a brown oil,
20 which was purified by flash column chromatography on silica gel (40-60) eluting with diethyl ether to give 6,8-dichloro-7-(2,4,6-trifluorophenyl)-pyrido[3,2-c]pyridazine as a yellow oil (0.015 g).

¹H NMR (CDCl₃) δ ppm: 6.92 (m,2H), 8.11 (d,1H), 9.71 (d,1H).

Step 5

25 Isopropylamine (0.5 ml) was added to the product from Step 4 (0.015 g) dissolved in DCM (1ml) containing dimethylacetamide (0.3 ml) in a sealed tube. The yellow solution became yellow/greenish. The vessel was then sealed and stirred at room temperature. The solvents were evaporated and the crude residue was purified using preparative thin layer chromatography silica gel plates eluting with ethyl acetate:hexane 1:1 to give two isomers:
30 [6-Chloro-7-(2,4,6-trifluorophenyl)-pyrido[3,2-c]pyridazin-8-yl]-isopropylamine (0.003 g).
¹H NMR (CDCl₃) δ ppm: 1.16 (d,6H), 3.41 (m,1H), 6.85 (dd,2H), 7.79 (bs,1H), 7.84 (d,1H), 9.40 (d,1H).

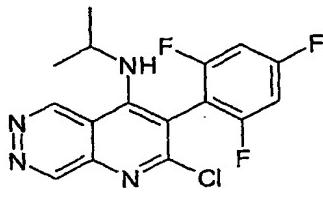
[8-Chloro-7-(2,4,6-trifluorophenyl)-pyrido[3,2-c]pyridazin-6-yl]-isopropylamine (0.005 g).

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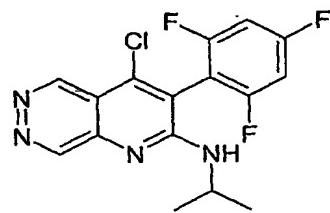
¹H NMR (CDCl₃) δ ppm: 1.24 (d,6H), 4.53 (m,1H), 4.73 (d,1H), 6.94 (dd,2H), 7.67 (d,1H), 9.25 (d,1H).

EXAMPLE 4

This Example illustrates the preparation of [2-chloro-3-(2,4,6-trifluorophenyl)-pyrido[2,3-d]pyridazin-4-yl]-isopropylamine (Compound No. 3, Table 21), and [4-chloro-3-(2,4,6-trifluorophenyl)-pyrido[2,3-d]pyridazin-2-yl]-isopropylamine (Compound No. 3, Table 117)



Compound No. 3, Table 21



Compound No. 3, Table 117

Step 1

5-Aminopyridazine-4-carboxylic acid ethyl ester (1.26 g, prepared according to *J. Het. Chem.*, (1968), 5, 845) was dissolved in dry toluene (125 ml) at 90°C, and DMAP (0.92 g) was added. 2,4,6-Trifluorophenylacetyl chloride (1.75 g of 95% purity material) was added dropwise with stirring at 70°C, and a white solid precipitated. The reaction was stirred at reflux for 5 hours and then filtered hot. The filtrate was evaporated to give 5-[2-(2,4,6-trifluorophenyl)-acetylamino]-pyridazine-4-carboxylic acid ethyl ester as a white solid (2.6 g), m.p. 143-144°C.

¹H NMR (CDCl₃) δ ppm: 1.45 (t,3H), 3.90 (s,2H), 4.45 (q,2H), 6.75 (m,2H), 9.45 (s1H), 10.60 (s,1H), 11.1 (bs,1H).

Step 2

The product from Step 1 (2.5 g) was dissolved in dry THF (50 ml) and the flask purged with nitrogen. Sodium bis-trimethylsilylamine (22.1 ml of a 1M solution in THF) was added dropwise with stirring at 0°C. A yellow precipitate appeared, and the reaction was stirred for 3 hours at 0°C. The reaction was quenched with concentrated hydrochloric acid (5 ml) at 0°C and then poured onto ice water, extracted with DCM and dried over magnesium sulphate. The solvent was evaporated to give 3-(2,4,6-trifluorophenyl)-1*H*-pyrido[2,3-d]pyridazine-2,4-dione as a yellow solid. Further product crystallised out of the aqueous solution overnight, to give a total yield of 1.29 g, m.p. >300°C.

¹H NMR (d⁶-DMSO) δ ppm: 7.25 (m,2H), 9.17 (s,1H), 9.47 (s,1H), 12.30 (bs,1H).

Step 3

The product from Step 2 (0.10 g) was heated to 90°C with phosphorus oxychloride (1.6 ml) with stirring. After 1 hour a clear yellow solution was obtained and the excess solvent was evaporated and ice water was added, giving a yellow solid. This was extracted 5 with DCM, and the solution dried over magnesium sulphate and evaporated to give 2,4-dichloro-3-(2,4,6-trifluorophenyl)-pyrido[2,3-d]pyridazine as a yellow foamy glass (0.11 g).
¹H NMR (CDCl₃) δ ppm: 6.90 (m,2H), 9.80 (s,1H), 10.0 (s, H).

Step 4

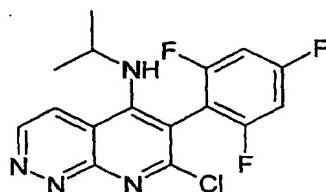
Isopropylamine (1.5 ml) was added to the product from Step 3 (0.020 g) in DCM and 10 the tube stoppered and the reaction stirred overnight at room temperature. The DCM was evaporated and water added to the residue, which was then extracted with DCM. The extract was dried over magnesium sulphate and evaporated to give an orange oil, which was purified by HPLC eluting with ethyl acetate:hexane 4:1 to give two isomers:

[2-Chloro-3-(2,4,6-trifluorophenyl)-pyrido[2,3-d]pyridazin-4-yl]-isopropylamine (0.007 g)
15 ¹H NMR (CDCl₃) δ ppm: 1.27 (d,6H), 4.05 (m,1H), 4.90 (bs,1H), 6.92 (m,2H), 9.55 (s,1H), 9.90 (s,1H).
[4-Chloro-3-(2,4,6-trifluorophenyl)-pyrido[2,3-d]pyridazin-2-yl]-isopropylamine (0.0055 g)
¹H NMR (CDCl₃) δ ppm: 1.25 (d,6H), 4.54 (m,1H), 4.67 (bs,1H), 6.90 (m,2H), 9.40 (s,1H), 9.50 (s,1H).

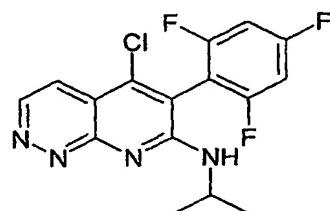
20

EXAMPLE 5

This Example illustrates the preparation of [7-chloro-6-(2,4,6-trifluorophenyl)-pyrido[2,3-c]pyridazin-5-yl]-isopropylamine (Compound No. 3, Table 26), and [5-Chloro-6-(2,4,6-trifluoro-phenyl)-pyrido[2,3-c]pyridazin-7-yl]-isopropylamine (Compound No.3, Table 122).



Compound No. 3, Table 26



Compound No. 3, Table 122

5 Step 1

3-Aminopyridazine-4-carboxylic acid (1.68 g, prepared as in JOC, (1985), 50, 346) was refluxed in ethanol (170 ml) with concentrated hydrochloric acid (2 ml) and *p*-toluen-

sulphonyl chloride (0.1 g) for 55 hours. The solvent was evaporated and ice water added to the residue, which was then neutralised with solid sodium bicarbonate. The mixture was extracted with chloroform, insoluble material filtered, the organic extract dried over magnesium sulphate and evaporated to give 3-aminopyridazine-4-carboxylic acid ethyl ester (1.02 g) as a white solid.

5 ^1H NMR (CDCl_3) δ ppm: 1.40 (t,3H), 4.40 (q,2H), 6.50 (bs,2H), 7.74 (d,1H), 8.72 (d,1H).

Step 2

The product from Step 1 (0.36g) was dissolved in dry toluene (25 ml) and DMAP (0.262 g) was added. A solution of 2,4,6-trifluorophenylacetyl chloride (0.45 g) in dry toluene (1 ml) was added dropwise with stirring, and a white precipitate formed. After stirring at room temperature for 10 minutes the reaction was stirred under reflux for 4.5 hours, and then allowed to stand overnight at room temperature. The white solid was filtered and washed with toluene, and the filtrate evaporated to give a brown oil, which was purified by HPLC eluting with ethyl acetate:hexane 4:1 to give 3-[2-(2,4,6-trifluorophenyl)-

10 acetylamino]-pyridazine-4-carboxylic acid ethyl ester as a pale yellow solid (0.57 g), m.p. 135°C.

15 ^1H NMR (CDCl_3) δ ppm: 1.40 (t,3H), 4.22 (s,2H), 4.41 (q,2H), 6.70 (m,2H), 7.94 (d,1H), 9.15 (d,1H), 10.30 (bs,1H).

Step 3

20 The product from Step 2 (2.0 g) was dissolved in dry THF (50 ml), and sodium bis(trimethylsilyl)amide (17.7 ml of a 1.0M solution in THF) was added dropwise with stirring under nitrogen at 0°C. The reaction was stirred for 3 hours at 0°C and a yellow precipitate was formed. The reaction was quenched with concentrated hydrochloric acid and then poured into ice water. The solid was filtered, washed with water and air dried to give 6-

25 (2,4,6-trifluorophenyl)-8*H*-pyrido[2,3-*c*]pyridazine-5,7-dione as a yellow solid (1.9 2g), m.p. >330°C, still containing some THF, which was used without further purification.

30 ^1H NMR ($\text{D}_6\text{-DMSO}$) δ ppm: 7.30 (m,2H), 8.10 (d,1H), 9.20 (d,1H), 11.90 (bs,1H), 12.60 (s,1H).

Step 4

35 The product from Step 3 (0.060 g) was heated to 90°C in phosphorus oxychloride (1 ml) for 1 hour to give a clear black solution. The mixture was cooled and the excess in phosphorus oxychloride evaporated. The residue was quenched with ice and aqueous sodium bicarbonate, extracted with ethyl acetate, the extract dried over magnesium sulphate and

- 80 -

evaporated to give 5,7-dichloro-6-(2,4,6-trifluorophenyl)-pyrido[2,3-c]pyridazine as a black solid (0.087 g).

¹H NMR (CDCl₃) δ ppm: 6.90 (m,2H), 8.30 (d,1H), 9.75 (d,1H).

Step 4

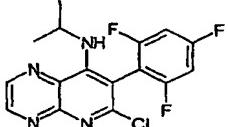
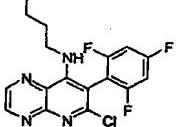
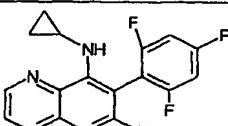
5 The product from Step 3 (0.080 g) was stirred with isopropylamine (2 ml) in DCM (5 ml) at room temperature overnight and then heated to 40°C in a sealed tube for 4 hours. The volatiles were evaporated, water was added and the mixture extracted with DCM. The extracts were dried over magnesium sulphate and evaporated to give a dark brown tar, which was purified by preparative TLC on silica gel plates eluting with ethyl acetate:hexane 3:2 to 10 give two isomers:

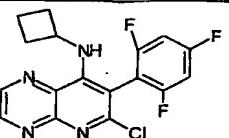
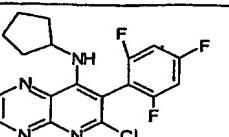
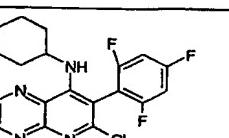
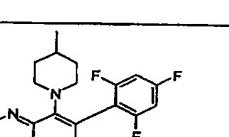
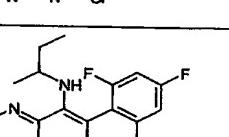
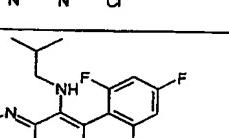
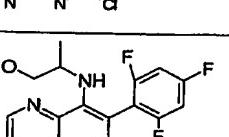
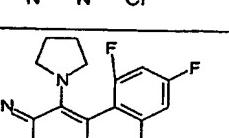
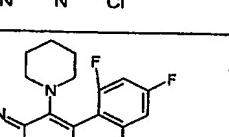
[5-chloro-6-(2,4,6-trifluoro-phenyl)-pyrido[2,3-c]pyridazin-7-yl]-isopropylamine as a gum (0.0014 g),

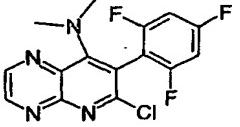
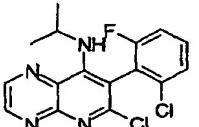
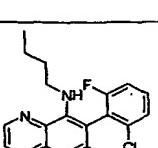
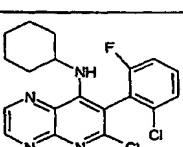
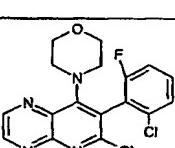
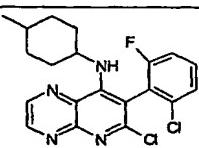
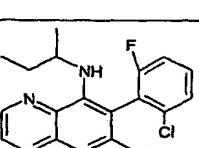
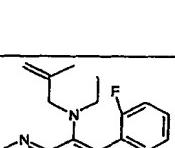
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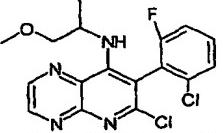
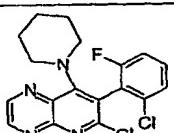
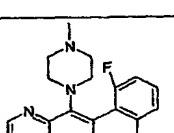
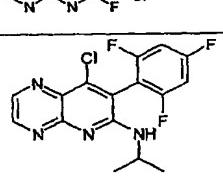
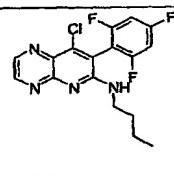
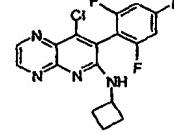
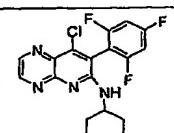
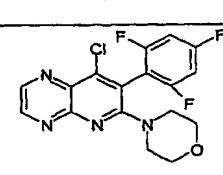
15 [7-Chloro-6-(2,4,6-trifluorophenyl)-pyrido[2,3-c]pyridazin-5-yl]-isopropylamine (0.008 g),
¹H NMR (CDCl₃) δ ppm: 1.20 (d,6H), 3.71 (m,1H), 4.45 (bs,1H), 6.87-6.92 (m,2H), 7.97 (d,1H), 9.37 (d,1H).

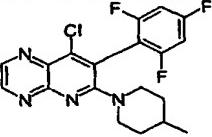
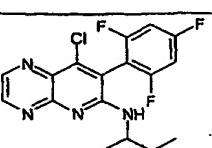
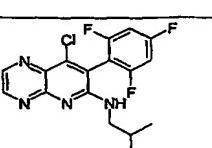
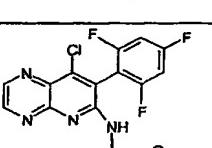
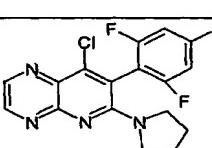
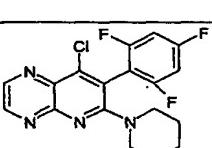
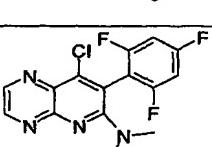
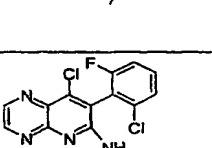
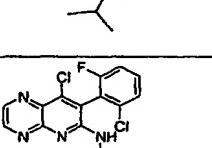
Table 133

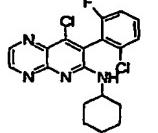
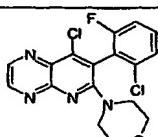
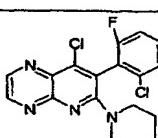
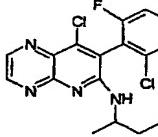
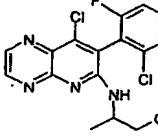
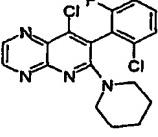
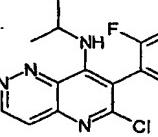
Compound No.	Table No.	Compound Structure	NMR data (ppm, in CDCl ₃ , unless otherwise stated) or Mpt.
3	1		1.1 (d,6H), 3.26 (m,1H), 6.84 (m,2H), 6.95 (bd,1H), 8.67 (d,1H), 9.0 (d,1H).
4	1		0.8 (t,3H), 1.27 (m,2H), 1.55 (m,2H), 2.87 (m,2H), 6.8,6.85 (ABd,2H); 8.66, 8.99 (ABd,2H).
14	1		129-131°C

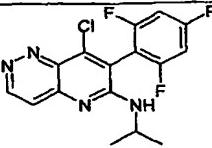
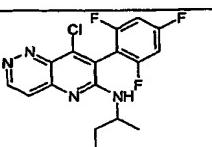
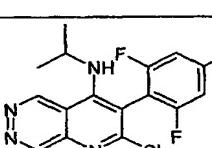
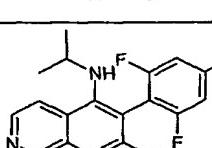
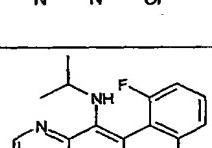
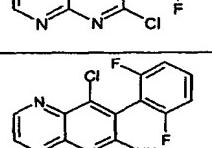
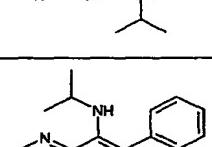
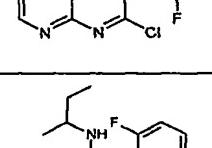
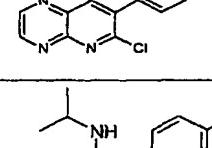
15	1		149-150 °C
16	1		175-177 °C
17	1		153-155 °C
22	1		0.92 (m) + 1.22 (m) + 1.55 (m) (total = 8H), 2.9 (m,2H), 6.85 (m,2H), 8.78,8.96 (ABd,2H).
23	1		151-153 °C
58	1		102-104 °C
108	1		1.12 (d,3H), 3.27 (m,2H), 3.3 (s,3H), 3.5 (m,1H), 6.8 (m,2H), 8.67 (d) + 8.97 (ABd) (total = 2H)
161	1		138-140 °C
162	1		140-141 °C

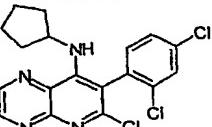
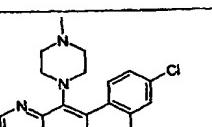
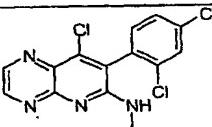
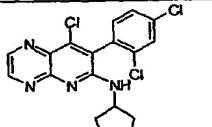
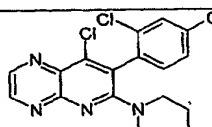
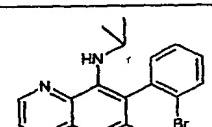
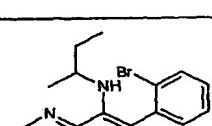
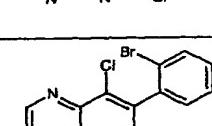
219	1		3.0 (s,6H), 6.85 (m,2H), 8.65,8.87 (ABd,2H)
3	5		157-159 °C
4	5		0.82 (m,3H), 1.22 m + 1.5 m (total = 4H), 2.82 (m,2H), 7.1-7.47 (m,3H), 8.67 + 9.05 (ABd,2H).
17	5		159-160 °C
20	5		166-168 °C
22	5		163-165 °C
23	5		163-165 °C
28	5		71-73 °C

108	5		1.05 (d) + 1.12 (d) (total = 3H), 3.1-3.5 (m,3H), 3.25 (d) + 3.32 (d) (total = 3H), 7.1 (m) + 7.4 (m) (total = 4H), 8.67 (d,1H), 9.06 (d,1H)
161	5		0.82 (m,4H), 3.65 (m,4H), 7.12-7.35 (m,3H), 8.66 + 8.87 (ABd,2H).
162	5		1.52 (m,6H), 3.3 (m,4H), 7.25 (m) + 7.4 (m) (total = 3H), 8.78 + 8.95 (ABd,2H).
171	5		2.3 (s,3H), 2.5 (m,4H), 7.15 (m,1H), 7.37 (m,2H), 8.75 (d,1H), 8.92 (d,1H).
3	6		1.25 (d,6H), 4.62 (bd,1H), 4.75 (m,1H), 6.67 (m,2H), 8.64 (d,1H), 8.85 (d,1H).
4	6		165-167 °C
15	6		214-216 °C
17	6		156-158 °C
20	6		3.4 (m,4H), 3.6 (m,4H), 6.9 (m,2H), 8.8 (d,1H), 8.95 (d,1H).

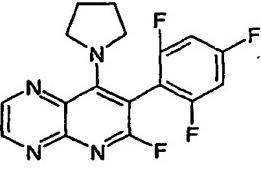
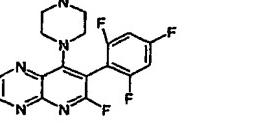
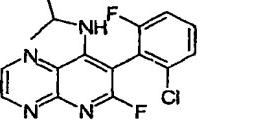
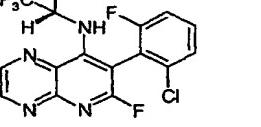
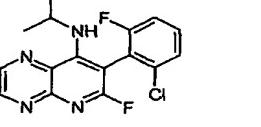
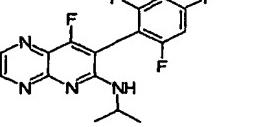
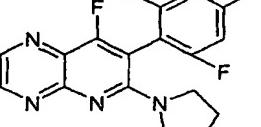
22	6		159-160 °C
23	6		145-147 °C
58	6		165-167 °C
108	6		1.27 (d,3H), 3.3 (s,3H), 3.47 (m,2H), 4.75 (m,H), 5.1 (bd,1H), 6.92 (m,2H), 8.64 (d, 1H), 8.85 (d,1H).
161	6		1.9m (4H); 3.4m (4H); 6.85m (2H); 8.62d (1H); 8.85d (1H)
162	6		1.4-1.55 (m,6H), 3.35 (m,4H), 6.87 (m,2H), 8.72 (d,1H); 8.92 (d,1H).
219	6		166-168 °C
3	10		155-157 °C
4	10		159-160 °C

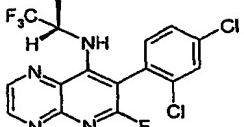
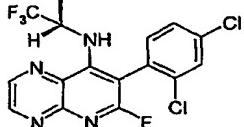
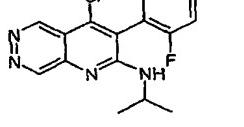
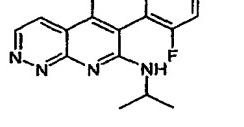
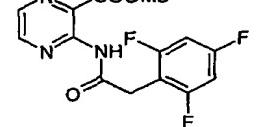
17	10		131-132 °C
20	10		171-173 °C
22	10		0.9 (d,3H), 0.87-1.1 (m,2H), 1.5 (m,3H), 2.87 (m,2H), 3.87 (m,2H), 7.17 (m) + 7.4 (m) (total = 3H), 8.72 (d,1H), 8.90 (d,1H).
23	10		0.87 (m) + 1.2 (m) + 1.5 (m) (total = 8H), 4.45 (bt,1H), 4.5 (m,1H), 7.25 (m) + 7.5 (m) (total = 3H), 8.63 (d,1H), 8.88 (d,1H).
108	10		1.25 (m,3H), 3.25 (d,3H), 3.45 (m,2H), 4.75 (m,1H), 5.0 (bt,1H), 7.22 (m) + 7.47 (m) (total = 3H), 8.64 (d,1H), 8.84 (d,1H).
161	10		177-179 °C
162	10		163-164 °C
3	11		1.16 (d,6H), 3.41 (m,1H), 6.85 (dd,2H), 7.79 (bs,1H), 7.84 (d,1H). 9.40 (d,1H).
23	11		0.79 (t,3H), 1.11 (d,3H), 1.47 (m,2H), 3.13 (m,1H), 6.86 (dd,2H), 7.79 (bs,1H), 7.84 (d,1H), 9.40 (d,1H).

3	16		1.24 (d,6H), 4.53 (m,1H), 4.73 (d,1H), 6.94 (dd,2H), 7.67 (d,1H), 9.25 (d,1H).
23	16		0.90 (t,3H), 1.20 (d,3H), 1.53 (m,2H), 4.38 (m,1H), 4.62 (d,1H), 6.95 (dd,2H), 7.63 (d,1H), 9.25 (d,1H).
3	21		1.27 (d,6H), 4.05 (m,1H), 4.90 (bs,1H), 6.92 (m,2H), 9.55 (s,1H), 9.90 (s,1H).
3	26		1.20 (d,6H), 3.71 (m,1H), 4.45 (bs,1H), 6.87-6.92 (m,2H), 7.97 (d,1H), 9.37 (d,1H).
3	31		1.25 (d,6H), 4.5 (bd,1H) 4.6 (m,1H), 7.15 (t,2H), 7.6 (m,1H), 8.625 (fd,1H), 8.85 (fd,1H).
665	31		1.10 (d,6H), 3.30 (m,1H), 6.90 (bd,1H), 7.05 (t,2H), 7.50 (m,1H), 8.65 (fd,1H), 9.0 (fd,1H).
3	32		1.10 (d,6H), 4.52 (m,2H), 7.28 (m,3H), 7.47 (m,1H), 8.52 (d,1H), 8.76 (d,1H)
23	32		0.78 (m,3H), 1.07 (m,3H), 1.45 (m,2H), 4.48 (m,2H), 7.25 (m,3H), 7.50 (m,1H), 8.51 (d,1H), 8.71 (d,1H)
3	37		160-161 °C

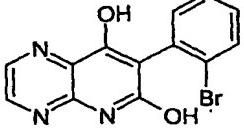
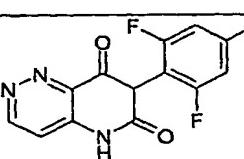
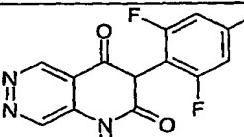
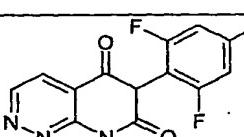
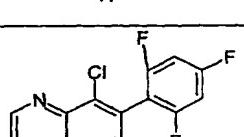
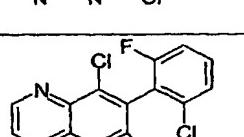
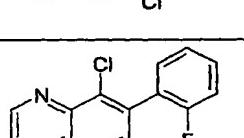
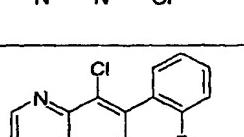
16	37		181-183 °C
171	37		2.3 (s,3H), 2.5 (m,3H), 3.2-3.5 (m,4H), 7.27 (m) + 7.4 (m) + 7.62 (m) (total = 3H), 8.77 (d,1H), 8.92 (d,1H).
665	37		0.92 (d,6H), 1.95 (m,1H), 3.37 (m) + 3.57 (m) (total = 2H), 4.67 (bt,1H), 7.27 (d) + 7.5 (m) + 7.67 (d) (total = 3H), 8.62 (d,1H), 8.95 (d,1H).
678	37		1.35 (m) + 1.62 (m) + 2.15 (m) (total = 8H), 4.6 (bd,1H), 4.75 (m,1H), 7.3 (m) + 7.5 (m) (total = 3H), 8.67 (d,1H), 8.87 (d,1H).
833	37		2.27 (s,3H), 2.35 (m,4H), 3.42 (m,4H), 7.3-7.6 (m,3H), 8.67 (d,1H), 8.92 (d,1H).
3	43		1.10 (d,6H), 4.32 (d,1H), 4.57 (m,1H), 7.22 (m,1H), 7.35 (m,1H), 7.48 (m,1H), 7.78 (m,H), 8.53 (d,1H), 8.71 (d,1H)
23	43		0.81 (m,3H), 1.10 (m,3H), 1.40 (m,2H), 4.26 (m,1H), 4.45 (m,1H), 7.25 (m,1H), 7.38 (m,1H), 7.50 (m,1H), 7.76 (m,1H), 8.52 (d,1H), 8.74 (d,1H)
685	43		0.62 (m,3H), 1.02 (m,3H), 1.32 (m,2H), 3.02 (m,1H), 6.42 (m,1H), 7.28 (m,1H), 7.46 (m,1H), 7.62 (m,1H), 7.69 (m,1H), 9.02 (d,1H), 9.10 (d,1H).

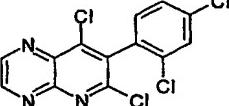
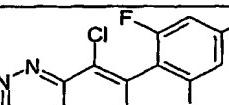
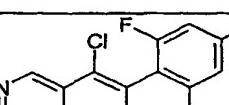
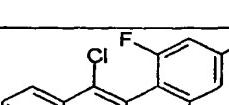
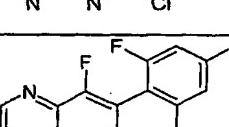
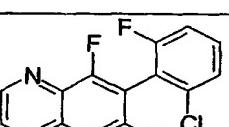
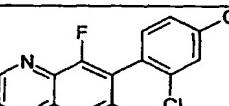
3	103		127-128°C
5	103		138-140°C
12	103		106-108 °C
14	103		120-121°C
15	103		153-154°C
23	103		101-102 °C
58	103		99-100 °C
92	103		1.07 (t,3H), 1.57 (s,3H), 3.52 (s,2H), 3.72 (q,2H), 4.85 (m,2H), 6.85 (m,2H), 8.8 (d,1H), 9.0 (d,1H).

161	103		148-150°C
171	103		167-160 °C
2651	103		100-101 °C
2660	103		1.3 (d,3H), 1.4 (d,3H), 3.9 (m,1H), 6.95-7.6 (m,4H), 8.75 (m,1H), 9.05 (m,1H).
2671	103		123-124°C
2706	103		0.8 (m,6H), 1.72 (m,1H), 2.6 (m,2H), 7.02 - 7.47 (m,4H), 8.6 (d,1H), 8.92 (d,1H).
3313	103		1.25 (m,6H), 4.5 (bd,1H), 4.67 (m,1H), 7.25 (m) + 7.5 (m) (total = 2H), 8.58 (d,1H), 8.83 (d,1H).
3471	103		151-152°C

43704	103		133-135 °C (diastereoisomer 1)
43704	103		137-139 °C (diastereoisomer 2)
43715	103		118-119 °C
43750	103		0.80 (d) + 0.83 (d) (total = 6H), 1.72 (m,1H), 2.65 (m,2H), 7.1-7.3 (m) + 7.35,7.6 (d) (total = 3H), 8.6 (d,1H), 8.92 (d,1H).
3	117		1.25 (d,6H), 4.54 (m,1H), 4.67 (bs,1H), 6.90 (m,2H), 9.40 (s,1H), 9.50 (s,1H).
3	122		1.27 (d,6H), 4.70-4.85 (bs + m, 2H), 6.95 (m,3H), 8.02 (d,1H), 9.22 (d,1H).
15	127		218-220°C
1	128		4.03 (s,5H), 6.74 (t,2H), 8.43 (d,1H), 8.61 (d,1H) 10.9 (s,1H).

6	128		162-163°C
12	128		158-159°C
13	128		1.48 (t,3H), 4.52 (q,2H), 6.73 (d,1H), 8.75 (d,1H).
25	128		1.45 (t,3H), 3.90 (s,2H), 4.45 (q,2H), 6.75 (m,2H), 9.45 (s1H), 10.60 (s,1H), 11.1 (bs,1H).
37	128		1.40 (t,3H), 4.22 (s,2H), 4.41 (q,2H), 6.70 (m,2H), 7.94 (d,1H), 9.15 (d,1H), 10.30 (bs,1H).
1	129		(d ⁶ -DMSO) 7.25(t,2H), 8.6(fd,1H), 8.7(fd,1H), 12.6(s,1H).
6	129		>220°C
9	129		250-252 °C

11	129		258 °C
12	129		>200 °C
13	129		(CD ₃ OD) 6.83 (2d,2H), 7.44 (d,1H), 9.00 (d,1H).
25	129		(d ⁶ -DMSO) 7.25 (m,2H), 9.17 (s,1H), 9.47 (s,1H), 12.30 (bs,1H).
37	129		(D ₆ -DMSO) 7.30 (m,2H), 8.10 (d,1H), 9.20 (d,1H), 11.90 (bs,1H), 12.60 (s,1H).
1	130		139-141 °C
6	130		154-155 °C
9	130		7.21(m,1H), 7.28(m,2H), 7.48(m,1H), 8.95(d,1H), 9.08(d,1H).
11	130		7.18(d, 1H), 7.29(m,1H), 7.41(t,1H), 7.69(dd,1H), 9.00(d,1H), 9.09(d,1H).

12	130		159-160°C
13	130		6.92 (m,2H), 8.11 (d,1H), 9.71 (d,1H).
25	130		6.90 (m,2H), 9.80 (s,1H), 10.0 (s, H).
37	130		6.90 (m,2H), 8.30 (d,1H), 9.75 (d,1H).
1	131		120-121°C
6	131		7.27 (m) + 7.55 (m) (total = 3H), 9.07 (d,1H), 9.2 (d,1H).
12	131		7.45 (m) + 7.67 (d) (total = 3H), 9.07 (d,1H), 9.2 (d,1H).

EXAMPLE 6

This Example illustrates the fungicidal properties of the compounds of the general formula (1).

Compounds were tested in a leaf disk assay, with methods described below. Test compounds were dissolved in DMSO, and diluted into water to 200 ppm.

Plasmopara viticola (downy mildew of grapevine): grapevine leaf disks were placed on agar in a 24-well plate and sprayed a solution of the test compound. After allowing to dry

completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed seven days after inoculation as preventive fungicidal activity.

5 *Phytophthora infestans* (late blight of potato on tomato): tomato leaf disks were placed on water agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

10 *Erysiphe graminis f.sp. hordei* (barley powdery mildew): barley leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

15 *Erysiphe graminis f.sp. tritici* (wheat powdery mildew): wheat leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

20 *Puccinia recondita f.sp. tritici* (wheat brown rust): wheat leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed nine days after inoculation as preventive fungicidal activity.

25 *Septoria nodorum* (wheat glume blotch): wheat leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

30 *Pyrenophora teres* (barley net blotch): barley leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

Pyricularia oryzae (rice blast): rice leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

Botrytis cinerea (grey mould): bean leaf disks were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

The following compounds gave greater than 60% control of disease:

Plasmopara viticola, Compounds 4 (1), 20 (1), 23 (5), 58 (6), 162 (6), 22 (10), 23 (10), 6 (120), 12 (120);

Phytophthora infestans, Compounds 3 (1), 58 (5), 162 (10), 3 (103);

Erysiphe graminis f.sp. hordei, Compounds 3 (1), 14 (1), 15 (1), 16 (1), 17 (1), 22 (1), 23 (1), 58 (1), 108 (1), 161 (1), 162 (1), 3 (5), 4 (5), 17 (5), 20 (5), 22 (5), 23 (5), 28 (5), 58 (5), 108 (5), 162 (5), 171 (5), 3 (6), 4 (6), 15 (6), 20 (10), 23 (10), 161 (10), 665 (31), 23 (32), 3 (37), 16 (37), 171 (37), 665 (37), 678 (37), 3 (43), 23 (43), 685 (43), 3 (103), 12 (103), 23 (103), 58 (103), 92 (103), 2651 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23844 (103) diastereoisomer 2, 23855 (103), 23890 (103);

Erysiphe graminis f.sp. tritici, Compounds 3 (1), 4 (1), 15 (1), 16 (1), 22 (1), 23 (1), 58 (1), 108 (1), 162 (1), 219 (1), 58 (95), 161 (5), 22 (6), 162 (10), 3 (31), 16 (37), 665 (37), 678 (37), 3 (103), 12 (103), 23 (103), 58 (103), 92 (103), 2651 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23844 (103) diastereoisomer 2, 23855 (103), 23890 (103);

Puccinia recondita f.sp. tritici, Compounds 3 (1), 14 (91), 15 (1), 16 (1), 17 (1), 23 (1), 58 (1), 108 (1), 161 (1), 162 (1), 4 (5), 17 (5), 23 (5), 28 (5), 58 (5), 108 (5), 162 (10), 3 (31), 16 (37), 665 (37), 678 (37), 3 (103), 12 (103), 23 (103), 58 (103), 92 (103), 2651 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23855 (103), 23890 (103);

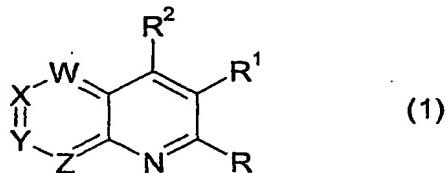
Septoria nodorum, Compounds 3 (91), 15 (1), 16 (1), 17 (1), 23 (1), 58 (1), 58 (95), 161 (5),

30 22 (6), 665 (37), 685 (43), 12 (103), 23 (103), 58 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23855 (103), 23890 (103);

Pyrenophora teres, Compounds 3 (1), 14 (1), 15 (1), 16 (1), 17 (1), 23 (1), 58 (1), 161 (1), 3 (5), 20 (5), 16 (37), 665 (37), 3 (103), 12 (103), 23 (103), 58 (103), 2651 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23855 (103), 23890 (103);
5 *Pyricularia oryzae*, Compounds 3 (1), 4 (1), 14 (1), 15 (1), 16 (1), 17 (1), 20 (1), 23 (1), 58 (1), 108 (1), 161 (1), 3 (5), 4 (5), 20 (5), 23 (5), 58 (5), 108 (5), 3 (6), 22 (6), 219 (6), 22 (10), 3 (32), 3 (37), 16 (37), 678 (37), 3 (43), 3 (103), 12 (103), 23 (103), 58 (103), 92 (103), 171 (103), 2651 (103), 2669 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23844 (103) diastereoisomer 2, 23855 (103), 23890 (103);
10 *Botrytis cinerea*, Compounds 4 (1), 14 (1), 15 (1), 16 (1), 17 (1), 22 (1), 58 (1), 108 (1), 4 (5), 22 (5), 28 (5), 58 (5), 108 (5), 162 (5), 3 (6), 3 (10), 16 (37), 678 (37), 23 (103), 92 (103), 2651 (103), 2660 (103), 23844 (103) diastereoisomer 2, 23855 (103), 23890 (103).

CLAIMS

1. The compound of the general formula (1):



5 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;

R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;

R and R² are independently H, halo, C₁₋₈ alkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio, C₂₋₈ alkenyl, C₂₋₈ alkynyl, cyano or NR³R⁴, provided that at least one of R and R² is NR³R⁴;

10 R¹ is halo, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C₁₋₄)alkyl, aryl(C₁₋₄)alkoxy, heteroaryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkoxy, aryl(C₁₋₄)-alkylthio, heteroaryl(C₁₋₄)alkylthio, morpholino, piperidino or pyrrolidino;

R³ and R⁴ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl,

15 C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₈)alkyl, NR⁵R⁶, provided that not both R³ and R⁴ are H or NR⁵R⁶, or

R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with one or more C₁₋₄ alkyl or C₁₋₄ alkoxy groups, or,

together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine,

20 thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring; and

R⁵ and R⁶ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₈)alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for

25 R⁸) being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆ alkoxy carbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or C₁₋₆ dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and

- any of the foregoing aryl or heteroaryl groups or moieties being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, 5 halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'''R''', -NHCOR'', -NHCONR''R''', -CONR''R''', -SO₂R'', -OSO₂R'', -COR'', -CR''=NR''' or -N=CR''R''', in which R''' and R'''' are independently hydrogen, C₁₋₄ alkyl, halo-(C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being 10 optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.
2. A compound according to claim 1 wherein W and Z are N and X and Y are CH.
- 15 3. A compound according to claim 1 or 2 wherein R² is NR³R⁴.
4. A compound according to claim 3 wherein R is halo.
5. A compound according to any one of the preceding claims wherein 20 R³ is C₁₋₈ alkyl, halo(C₁₋₈)alkyl, hydroxy(C₁₋₈)alkyl, C₁₋₄ alkoxy(C₁₋₈)alkyl, C₁₋₄ alkoxyhalo(C₁₋₈)alkyl, tri(C₁₋₄)alkylsilyl(C₁₋₆)alkyl, C₁₋₄ alkylcarbonyl(C₁₋₈)alkyl, C₁₋₄ alkylcarbonylhalo(C₁₋₈)alkyl, phenyl(C₁₋₄)alkyl, C₂₋₈ alkenyl, halo(C₂₋₈)alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl optionally substituted with chloro, fluoro or methyl, C₃₋₈ cycloalkyl(C₁₋₄)alkyl, phenylamino, piperidino or morpholino, the phenyl ring of 25 phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy and halo-(C₁₋₄)alkoxy; and
- R⁴ is H, C₁₋₄ alkyl, halo(C₁₋₄)alkyl or amino, or
- 30 R³ and R⁴ together form a C₃₋₇ alkylene or alkenylene chain optionally substituted with methyl, or, together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide

ring or a piperazine or piperazine *N*-(C₁₋₄)alkyl (especially *N*-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl.

6. A compound according to any one of the preceding claims wherein
5 R¹ is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkoxy, pyridyl optionally substituted with from one to four halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkoxy, 2- or 3-thienyl optionally substituted with from one to three halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkoxy, or piperidino or morpholino both optionally substituted with one or two methyl groups.
10
7. A compound according to claim 6 wherein R¹ is 2,6-difluorophenyl, 2-fluoro-6-chlorophenyl, 2,5,6-trifluorophenyl, 2,4,6-trifluorophenyl, 2,6-difluoro-4-methoxyphenyl or pentafluorophenyl.
15
8. A compound according to claim 1 wherein
W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;
20 R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl; one of R and R² (preferably R²) is NR³R⁴ and the other is halo; R¹ is halo, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)-alkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C₁₋₄)alkyl, aryl(C₁₋₄)alkoxy, heteroaryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkoxy, aryl(C₁₋₄)alkylthio, heteroaryl(C₁₋₄)alkylthio, morpholino, piperidino or pyrrolidino;
25 R³ and R⁴ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)-alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₈)alkyl, NR⁵R⁶, provided that not both R³ and R⁴ are H or NR⁵R⁶, or
30 R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with one or more C₁₋₄ alkyl or C₁₋₄ alkoxy groups, or, together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide

ring or a piperazine or piperazine *N*-(C₁₋₄)alkyl (especially *N*-methyl) ring; and R⁵ and R⁶ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)-alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₈)alkyl; any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R⁸) being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆ alkoxycarbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or C₁₋₆ dialkylamino,
any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and any of the aryl, heteroaryl, aryloxy or heteroaryl groups being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoxyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR"⁹R"¹⁰, -NHCOR"¹¹, -NHCONR"¹²R"¹³, -CONR"¹⁴R"¹⁵, -SO₂R"¹⁶, -OSO₂R"¹⁷, -COR"¹⁸, -CR"¹⁹=NR"²⁰ or -N=CR"²¹R"²², in which R"⁹ and R"¹⁰ are independently hydrogen, C₁₋₄ alkyl, halo-(C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.

9. A compound according to claim 1 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;
R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;
one of R and R² (preferably R²) is NR³R⁴ and the other is halo;
R¹ is halo, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)-alkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C₁₋₄)alkyl, aryl(C₁₋₄)alkoxy, heteroaryl(C₁₋₄)alkyl, heteroaryl-(C₁₋₄)alkoxy, aryl(C₁₋₄)alkylthio, heteroaryl(C₁₋₄)alkylthio, morpholino, piperidino or pyrrolidino;
R³ is C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₂₋₄ alkenyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)-alkyl or phenylamino in which the phenyl ring is optionally substituted with one, two or three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy and

- halo(C₁₋₄)alkoxy; and R⁴ is H, C₁₋₄ alkyl or amino, or
R³ and R⁴ together form a C₄₋₆ alkylene chain optionally substituted with C₁₋₄ alkyl or
C₁₋₄ alkoxy, or,
together with the nitrogen atom to which they are attached, R³ and R⁴ form a
5 morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide
ring or a piperazine or piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring;
any of the alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R⁸)
being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆
10 alkoxycarbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or
C₁₋₆ dialkylamino,
any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and
pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and
any of the aryl or heteroaryl groups or moieties being optionally substituted with one
or more substituents selected from halo, hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl,
15 C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo-
(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)-
alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoyloxy,
cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR["]R^{"",} -NHCOR^{"",}
-NHCONR["]R^{"",} -CONR["]R^{"",} -SO₂R^{"",} -OSO₂R^{"",} -COR^{"",} -CR^{""}=NR^{"",} or
-N=CR["]R^{"",} in which R["] and R^{"",} are independently hydrogen, C₁₋₄ alkyl, halo-
20 (C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆
cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being
optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.
- 25 10. A compound according to claim 1 wherein
W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;
R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;
R and R² are independently H, halo, C₁₋₈ alkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio, C₂₋₈
30 alkenyl, C₂₋₈ alkynyl, cyano or NR³R⁴, provided that at least one of R and R²
(preferably R²) is NR³R⁴;
R¹ is optionally substituted phenyl;
R³ and R⁴ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)-
alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₈)alkyl,

NR⁵R⁶, provided that not both R³ and R⁴ are H or NR⁵R⁶, or
R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally
substituted with one or more C₁₋₄ alkyl or C₁₋₄ alkoxy groups, or,
together with the nitrogen atom to which they are attached, R³ and R⁴ form a
5 morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide
ring or a piperazine or piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring; and
R⁵ and R⁶ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)-
alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₈)alkyl;
any of the alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R⁸)
10 being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆
alkoxycarbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or
C₁₋₆ dialkylamino,
any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and
15 pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and
any of the aryl or heteroaryl groups or moieties, including the phenyl group of R¹,
being optionally substituted with one or more substituents selected from halo,
hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy,
20 C₂₋₆ alkynyoxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio,
hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl,
phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro,
-NR["]R^{"",} -NHCOR^{"",} -NHCONR["]R^{"",} -CONR["]R^{"",} -SO₂R^{"",} -OSO₂R^{"",} -COR^{"",}
25 -CR^{"=}NR^{"",} or -N=CR["]R^{"",}, in which R["] and R^{"",} are independently hydrogen, C₁₋₄
alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl,
C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being
optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.

11. A compound according to claim 1 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;

R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;

30 R is H, halo, C₁₋₄ alkyl), C₁₋₄ alkoxy or cyano;

R¹ is phenyl optionally substituted with from one to five halogen atoms or with from
one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or
halo(C₁₋₄)alkoxy, pyridyl optionally substituted with from one to four halogen atoms

or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkoxy, 2- or 3-thienyl optionally substituted with from one to three halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkoxy, or piperidino or morpholino both optionally substituted with one or two methyl groups;

5 R² is NR³R⁴;

R³ is C₁₋₈ alkyl, halo(C₁₋₈)alkyl, hydroxy(C₁₋₈)alkyl, C₁₋₄ alkoxy(C₁₋₈)alkyl, C₁₋₄ alkoxyhalo(C₁₋₈)alkyl, tri(C₁₋₄)alkylsilyl(C₁₋₆)alkyl, C₁₋₄ alkylcarbonyl(C₁₋₈)alkyl, C₁₋₄ alkylcarbonylhalo(C₁₋₈)alkyl, phenyl(C₁₋₄)alkyl, C₂₋₈ alkenyl, halo(C₂₋₈)alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl optionally substituted with chloro, fluoro or methyl, C₃₋₈ cycloalkyl(C₁₋₄)alkyl, phenylamino, piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy and halo(C₁₋₄)alkoxy; and

10 R⁴ is H, C₁₋₄ alkyl, halo(C₁₋₄)alkyl or amino, or

R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with methyl, or, together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine N-(C₁₋₄)alkyl (especially N-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl

12. A compound according to claim 1 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR⁸;

25 R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;

R is halo;

R¹ is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkoxy;

30 R² is NR³R⁴;

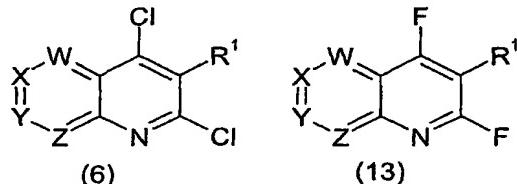
R³ is C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₂₋₄ alkenyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)-alkyl or phenylamino in which the phenyl ring is optionally substituted with one, two or three substituents selected from halo, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy and

halo(C₁₋₄)alkoxy; and

R^4 is H, C₁₋₄ alkyl or amino, or R^3 and R^4 together form a C₄₋₆ alkylene chain optionally substituted with methyl, or, together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine ring.

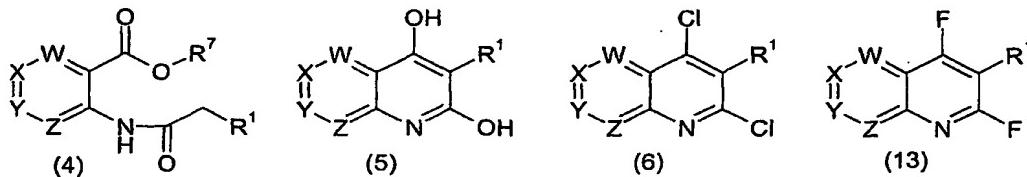
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13. A process for preparing a compound of the general formula (1) according to claim 1 wherein one of R and R² is chloro or fluoro and the other is NR³R⁴ and W, X, Y, Z, R¹, R³ and R⁴ are as defined in claim 1, which comprises reacting an amine of the general formula NR³R⁴ with a compound of the general formula (6) or (13):



10

14. The intermediate chemicals having the general formulae (4), (5), (6) and (13):



15

wherein W, X, Y, Z and R¹ are as defined in claim 1 and R⁷ is C₁₋₄ alkyl.

15. A plant fungicidal composition comprising a fungicidally effective amount of a compound as defined in claim 1 and a suitable carrier or diluent therefor.

20 16. A method of combating or controlling phytopathogenic fungi which comprises applying to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or to any other plant growth medium, a fungicidally effective amount of a compound according to claim 1 or a composition according to claim 15.

AMENDED CLAIMS

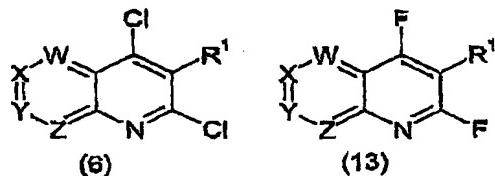
[Received by the International Bureau on 13 May 2004 (13.05.04): original claim 14 amended; remaining claims unchanged; (1 page)]

halo(C₁₋₄)alkoxy"; and

R^4 is H, C₁₋₄ alkyl or amino, or R^3 and R^4 together form a C₄₋₆ alkylene chain optionally substituted with methyl, or, together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine ring.

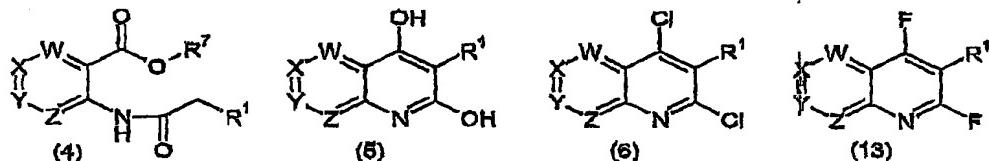
5

13. A process for preparing a compound of the general formula (1) according to claim 1 wherein one of R¹ and R² is chloro or fluoro and the other is NR³R⁴ and W, X, Y, Z, R¹, R³ and R⁴ are as defined in claim 1, which comprises reacting an amine of the general formula NR³R⁴ with a compound of the general formula (6) or (13);



10

14. The intermediate chemicals having the general formulae (4), (5), (6) and (13):



15

wherein W, X, Y, Z and R¹ are as defined in claim 1 and R⁷ is C₁₋₄ alkyl, other than the compound of formula (6), wherein X and Y are N, W and Z are C—Cl and R¹ is Cl

20

15. A plant fungicidal composition comprising a fungicidally effective amount of a compound as defined in claim 1 and a suitable carrier or diluent therefor.
 16. A method of combating or controlling phytopathogenic fungi which comprises applying to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or to any other plant growth medium, a fungicidally effective amount of a compound according to claim 1 or a composition according to claim 15.

25

INTERNATIONAL SEARCH REPORT

Application No
PCT/GB 03/05250

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D47/04 A01N43/90

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 821 244 A (BRAUN PETER ET AL) 13 October 1998 (1998-10-13) Abstract; columns 1-3; column 14, line 56 to column 15, line 4.	1-12, 15, 16
X	DATABASE BEILSTEIN BEILSTEIN INSTITUTE FOR ORGANIC CHEMISTRY, FRANKFURT-MAIN, DE; XP002272856 Database Accession No. 538395 (BRN). & CROAT. CHEM. ACTA, vol. 44, 1972, pages 419-421,	14
Y	WO 02/083676 A (BASF AG ; ALBERT GUIDO (DE); REHNIG ANNEROSE (DE); AMMERMANN EBERHARD) 24 October 2002 (2002-10-24) cited in the application Abstract; claims 1-8.	1-12, 15, 16
	-/-	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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Date of the actual completion of the International search

Date of mailing of the International search report

9 March 2004

29/03/2004

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INTERNATIONAL SEARCH REPORT

Application No
PCT/GB 03/05250

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 1 249 452 A (BASF AG) 16 October 2002 (2002-10-16) cited in the application Abstract; claims 1-6. -----	1-12, 15, 16
A	GB 1 431 063 A (SQUIBB & SONS INC) 7 April 1976 (1976-04-07) Claims 1-15, page 2, right column, lines 58-91. -----	1-16

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Application No PCT/GB 03/05250	
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